Medical Policy

Subject:	Products for Wound Healing and Soft Tissue Grafting: Investigational		
Document #:	SURG.00011	**Publish Date:**	07/01/2025
Status:	Revised	**Last Review Date:**	05/08/2025

Description/Scope

This document addresses soft tissue (e.g., skin, ligament, cartilage, etc.) substitutes which are considered investigational.

Note: This document does not address:
- The use of fresh, unfrozen, unprocessed allogeneic cadaver-derived skin grafts (see definition section for more information); or
- The use of meshes or patches when used for hernia repair procedures; or
- Products used to treat osteochondral defects (for information on such products, please refer to the applicable guidelines used by the plan).

Note: For additional information please see:
- ANC.00007 Cosmetic and Reconstructive Services: Skin Related
- ANC.00008 Cosmetic and Reconstructive Services of the Head and Neck
- CG-SURG-123-Autologous Fat Grafting and Injectable Soft Tissue Fillers
- CG-SURG-127 Products for Wound Healing and Soft Tissue Grafting: Medically Necessary Uses
- MED.00110 Silver-based Products for Wound and Soft Tissue Applications
- MED.00132 Autologous Adipose-derived Regenerative Cell Therapy
- SURG.00023 Breast Procedures; including Reconstructive Surgery, Implants and Other Breast Procedures
- TRANS.00035 Therapeutic use of Stem Cells, Blood and Bone Marrow Products

Note: See definition section for information on The Women's Health and Cancer Rights Act of 1998 (WHCRA).

Position Statement

Investigational and Not Medically Necessary

The following products are considered **investigational and not medically necessary** for all uses:
1. Abiomend
2. Abiomend hydromembrane
3. Abiomend Xplus membrane
4. Abiomend Xplus hydromembrane
5. ACApatch™
6. Ac5 advanced wound system
7. Acesso
8. Acesso AC

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9. Acesso DL
10. Acesso TL
11. ACM Extra Surgical Collagen
12. ACM Extra Surgical Collagen Powder
13. ACM Surgical Collagen
14. Actishield™
15. ActiveBarrier®
16. ActiveMatrix®
17. Aesten Inject (see MegaDerm®)
18. Affinity™
19. AlloGen-LI™
20. AlloGen™
21. AlloMax™
22. AlloMend™
23. AlloPatch® Pliable
24. alloPLY™
25. Alloskin AC
26. AlloSkin RT
27. AlloWrap®
28. AlloWrap™ Dry
29. AlloWrap™ DS
30. Alphaplex™ with MariGen Omega3™
31. AltiPly™
32. AmbientFactor™
33. Ambio5®
34. AmchoPlast
35. AmchoPlast FD
36. American amnion
37. American amnion AC
38. American amnion AC tri-layer
39. AmniCore Pro+
40. Amnio Burgeon Dual-Layer Membrane
41. Amnio Burgeon Membrane
42. Amnio Burgeon Hydromembrane
43. Amnio Burgeon X-Membrane Dual Layer
44. Amnio Burgeon Xplus Membrane
45. Amnio Burgeon Xplus Hydromembrane
46. AmnioCore SL
47. Amnio FRT™
48. Amnio F™
49. Amnio Quad-Core
50. Amnio Restore™
51. Amnio Tri-Core amniotic
52. Amnio wound
53. AmnioAMP-MP

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54. AmnioAMP-PF
55. AmnioAMP-X
56. AmnioArmor®
57. AmnioBind
58. AmnioCare®
59. AmnioClear®
60. AmnioCord®
61. AmnioCore
62. AmnioCore Pro
63. AmnioCyte
64. AMNIOEXCEL™
65. Amniofill®
66. AmnioFix™
67. Amnioflex™
68. AmnioGuard®
69. AmnioHeal®
70. AmnioMatrix™
71. AmnioMTM™
72. Amniopro™
73. AMNIOREPAIR™
74. Amnios®
75. Amnios® RT
76. AmnioShield®
77. Amniostrip™
78. Amniotext
79. AmnioTX™
80. Amniovo™ (Solo, Dual, and Matrix)
81. Amniovo™ Max
82. Amniowrap2™
83. Amniply
84. AmnyoFactor™
85. AmnyoFluid™
86. Anu RHEO™
87. Aongen™ Collagen Matrix
88. Apis®
89. Architect Extracellular Matrix™
90. ArdeoGraft
91. AROA ECM™
92. Artacent® AC Powder
93. Artacent® cord
94. Artacent® Flex
95. Artacent® Wound
96. Artelon®
97. Arthrex® Amnion matrix
98. ArthroFlex™

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99. ARTIA™ Reconstructive Tissue Matrix
100. Ascent®
101. Atlas Wound Matrix
102. Avance® Nerve Graft
103. Avaulta Plus™
104. Avive®
105. AxoBioMembrane
106. Axograft™
107. AxoGuard® nerve connector
108. AxoGuard® nerve protector
109. Axolotl Ambient™
110. Axolotl Cryo™
111. Axolotl DualGraft™
112. Axolotl Graft™
113. Axolotl Shot™
114. BEAR® (Bridge-Enhanced ACL Repair) Implant
115. BellaCell HD
116. Belladerm®
117. BellaGen™
118. BioBrace™ Implant
119. Bio-ConneKt®
120. BioDDryFlex® Resorbable Adhesion Barrier
121. Biodesign Nipple Reconstruction Cylinder
122. BioDExCel™
123. BioDFactor™
124. BioDFence™
125. BioDOptix™
126. Bioengineered autologous skin-derived products (for example, SkinTE™, MyOwn Skin™)
127. BioFiber™
128. BioFix
129. BioSkin® Flow Amniotic Wound Matrix
130. Biotape XM Tissue Matrix
131. BioWound
132. BioWound plus
133. BioWound Xplus
134. Cardiamend™
135. CardioCel®
136. CardioGRAFT®
137. CaregraFT™
138. Celera Dual Layer™
139. Celera Dual Membrane™
140. CellerateRX®
141. Cellesta amnion granulate
142. Cellesta amniotic membrane
143. Cellesta cord

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144. Cellesta flowable amnion
145. Cellesta™ Amniotic Membrane
146. CG CryoDerm™
147. Choriply
148. CLARIX™ 100 Quick-Peel Wound Matrix
149. CLARIX™ 1k
150. CLARIX™ FLO
151. Cocoon Membrane
152. Cogenex Amniotic Membrane
153. Cogenex Flowable Amnion
154. CollaFilm®
155. CollaFix™
156. CollaGUARD®
157. CollaMend™
158. COLLARX®
159. CollaSorb™
160. CollaWound™
161. Coll-e-Derm™
162. Collexa®
163. Collieva®
164. Complete AA
165. Complete ACA
166. Complete FT
167. Complete SL
168. Conexa™
169. Connext™ Surgical Matrix
170. CoreCyte™
171. Coreleader Colla-Pad
172. Coretext™
173. CorMatrix®
174. Corova
175. Corplex™
176. C-QUR™
177. CRXa™
178. Cryo-Cord™
179. CryoMatrix®
180. CryoSkin®
181. Cuffpatch™
182. Cygnus Disk
183. CYGNUS Matrix™
184. CYGNUS Max™
185. CYGNUS Solo™
186. Cymetra®
187. Cytal® Burn Matrix (formerly MatriStem)
188. Cytal® Multilayer Matrix (formerly MatriStem)

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189. Cytal® Wound Matrix (formerly MatriStem)
190. Cytoflex®
191. Cytoplast™
192. DeNovo® NT Graft
193. DermaBind CH
194. DermaBind FM™
195. DermaBind SL
196. Dermacyte™ Amniotic Wound Matrix
197. DermADAPT™ Wound Dressing
198. Derma-Gide®
199. DermaPure™
200. DermaSpan™
201. Dermavest 2™
202. Dermavest™
203. DermMatrix
204. Derm-Maxx
205. DuoAmnion™
206. DressSkin™
207. DuraSorb®
208. DuraForm™
209. Duragen® XS
210. Duragen™ Plus
211. DuraMatrix™
212. DuraMatrix-Onlay®
213. DuraMatrix-Onlay® Plus
214. DuraMatrix Suturable®
215. Durepair® Regeneration Matrix
216. E-Graft™
217. Emerge Matrix
218. Enclose TL Matrix
219. Endobon® Xenograft Granules
220. Endoform® Antimicrobial
221. Endoform® Natural Dermal Template
222. ENDURAgen™
223. Enverse®
224. EpiBurn
225. EpiDex®
226. EpiFix™, particulate or injectable form
227. EpiFlex®
228. EpiXpress
229. Excellagen®
230. Fibro-Gide®
231. FloGraft™
232. FlowerDerm™
233. FlowerFlo™ (FlowerAmnioFlo)

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234. FlowerPatch™ (FlowerAMINOPatch)
235. Fluid flow™
236. Fluid GF™
237. FortaDerm™ Wound Dressing (see PuraPly™)
238. Fortiva™ Porcine Dermis
239. GalaFLEX®
240. GalaFORM®
241. GalaSHAPE® 3D
242. Gammagraft™
243. Genesis amniotic membrane
244. Gentrix® Surgical Matrix
245. GENTRIX™
246. GORE BIO-A® Fistula Plug
247. Gore® Acuseal Cardiovascular Patch
248. Grafix plus
249. Grafix® CORE
250. Graftjacket™ Xpress injectable
251. GraftJacket™, injectable form
252. GraftRope™
253. HA Absorbent Wound Dressing
254. Helicoll®
255. HeliMEND
256. Helisorb®
257. hMatrix®
258. Human health factor 10™ amniotic patch (hhf10-p)
259. Hyalomatrix®
260. Impax Dual Layer
261. Inforce®
262. InnovaBurn®
263. InnovaMatrix® PD
264. InnovaMatrix® AC
265. InnovaMatrix® FS
266. Integra® Flow
267. InteguPly™
268. Interfy
269. Jaloskin®
270. Keramatrix®
271. Kerasorb®
272. KeraSys™
273. Keroxx Flowable Wound Matrix
274. Lamellas
275. Lamellas XT
276. LiquidGen™
277. Lyoplant® (See Tutopatch)
278. Mantle DL Matrix

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279. MariGen Shield
280. MatrACELL®
281. MatriDerm®
282. Matrion
283. MatriStem®
284. Matrix HD™
285. MatrixDerm™ (see Cytal)
286. Medeor™
287. MediHoney®
288. Mediskin®
289. MegaDerm™
290. MegaDerm™ HD
291. MegaFill
292. MegaSheet
293. Membrane Graft™
294. Membrane Patch™
295. Membrane Wrap ™
296. Membrane Wrap-Hydro
297. Memoderm™
298. Menaflex™ Collagen Meniscus Implant
299. Meso BioMatrix™
300. MIAMNION®
301. Microlyte matrix®
302. Miro3D
303. MIRODERM™
304. Miromatrix Biological Mesh
305. Miromesh®
306. MiroTract® Wound Matrix
307. MLG-Complete
308. MOST™
309. MyOwn Skin
310. Myriad Matrix™
311. Myriad Morcells™
312. Nanofactor™ Flow
313. Nanofactor™ Membrane
314. Neoform Dermis™
315. NeoMatriX
316. Neopatch
317. Neostim DL
318. Neostim membrane
319. Neostim TL
320. NEOVEIL® sheet
321. Neox RT®
322. NEOX® 100 Quick-Peel Wound Matrix
323. NEOX® 1k Wound Matrix

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324. NEOX® FLO
325. Neuragen® Nerve Guide
326. Neuragen® Nerve Wrap
327. Neuro-Patch
328. NeuraWrap™
329. Neuroflex™
330. NeuroMatrix™
331. NeuroMend™
332. NEVELIA® bi-layer matrix
333. Novachor
334. Novafix™
335. Novomaix Rebound Matrix
336. Novosorb™ Biodegradable Temporizing Matrix (BMT)
337. NuCel®
338. NuDyn™
339. Oasis Burn Matrix
340. Ologen™ Collagen Matrix
341. Omeza Collagen Matrix
342. OrthADAPT™
343. Orthoflow
344. OsseoGuard®
345. Ovation®
346. Overlay SL Matrix
347. PalinGen dual-layer membrane
348. PalinGen Flow™
349. PalinGen SportFlow™
350. PalinGen® Xplus Hydromembrane
351. PalinGen® Xplus Membrane
352. Palisade DM Matrix
353. PelloGraft
354. Pelvicol®
355. PelviSoft®
356. Pericol®
357. Peri-Guard® Repair Patch
358. Peri-Strips Dry®
359. Permacol™
360. PermeaDerm B
361. PermeaDerm C
362. PermeaDerm Glove
363. Phoenix™ Wound Matrix
364. PhotoFix® Decellularized Bovine Pericardium
365. Plurivest®
366. PolyCyte™
367. Preclude® Pericardial Membrane
368. Preclude® Vessel Guard

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369. Procenta®
370. ProgenaMatrix™
371. ProLayer
372. ProMatrX ACF
373. Promogran™
374. Protext™
375. PTFE felt
376. Puracol®
377. PuraPly™ (see Fortaderm)
378. Puros® Dermis
379. PX50® and X50® Plus
380. Rampart DL Matrix
381. Rebound™ Matrix
382. Reeva FT
383. RegeneLink Amniotic Membrane allograft
384. RegenePro™
385. RegenSeal
386. REGENETEN™
387. REGUaRD
388. RenoGraft
389. Renuva®
390. Repliform®
391. Repriza™
392. Resolve Matrix™
393. Restrata MiniMatrix, 5 mg
394. Restore® Orthobiologic Soft Tissue Implant
395. Restorigin
396. Restrata®
397. REVITA®
398. Revita®
399. Revitalon™
400. RevoShield + Amniotic Barrier
401. Rx Flow
402. Rx Membrane
403. SanoGraf
404. SanoGraf™
405. Sanopellis
406. Seamguard®
407. Sentry SL Matrix
408. SERAGYN® BR
409. SERASYNTH® MESH BR
410. SERI® Surgical Scaffold
411. Shelter DM Matrix
412. Signature A Patch
413. SIS Wound Dressing II

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414. SJM™ Pericardial Patch
415. SkinTE
416. SportMatrix
417. SportMesh™
418. SS Matrix™
419. SteriGraft™
420. SteriMatrix™
421. SteriShield™
422. Stimulen™ Collagen
423. SUPRA SDRM®
424. Suprathel®
425. SureDerm®
426. SurFactor®
427. SurGraft®
428. SurGraft FT
429. SurGraftXL
430. SurgiCord™
431. surgiGRAFT™
432. surgiGRAFT™ nano
433. surgiGRAFT™-Dual
434. Surgisis® (including Surgisis® AFP™ Anal Fistula Plug, Surgisis® Gold™ Hernia Repair Grafts, and Surgisis® Biodesign™)
435. Symphony™
436. Talymed™
437. TAPESTRY® RC
438. tarSys™
439. TenoGlide™
440. TenSIX™
441. TheraForm™ Standard/Sheet
442. TheraGenesis®
443. TIGR Matrix Surgical Mesh
444. TiLOOP® Bra
445. TissueMend®
446. Tornier® BioFiber Absorbable Biological Scaffold
447. TOTAL™
448. TranzGraft®
449. TruSkin™
450. Tutomesh™ Fenestrated Bovine Pericardium
451. Tutopatch™ Bovine Pericardium
452. Unite™
453. Vascu-Guard®
454. Vendaje (Other than for ocular indications.)
455. Veritas® Collagen Matrix
456. VersaShield™
457. VersaWrap®

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458. VIA DERMIS™
459. Via Disc® NP
460. Viable Allograft Supplemental Disc Regeneration (VAST)
461. Viaflow
462. VIAGENEX®
463. VIA Matrix
464. VICRYL™ Mesh
465. VIM® human amniotic membrane
466. VitoGraft
467. WoundEx®
468. Woundfix Plus
469. Woundfix Xplus
470. Woundfix,
471. WoundFix™
472. WoundPlus™
473. Xceed™
474. Xcellistem®
475. XCM Biologic™
476. Xelma®
477. XenMatrix™ Surgical Graft
478. XenoSure® Biologic Patch
479. X-Repair
480. Xwrap™ (Hydro, DRY, and ECM)
481. Xwrap Dual
482. Xwrap Plus
483. Zenith™ human amniotic membrane.

Rationale

General considerations

There are many different products (see definition section for product types) available for soft tissue grafting and wound treatment. These products differ in source (e.g., human cadaveric, synthetic, bovine, porcine, equine, a combination of several types, etc.), tissue (e.g., dermis, pericardium, intestinal mucosa, etc.), bioburden reduction (e.g., nonsterile, sterile), additives (e.g., antibiotics, surfactants), delivery formats (e.g., wet packaged, freeze-dried), and preparation requirements (e.g., multiple rinses, rehydration). Additionally, products are often procured, produced, manufactured, or processed in sufficiently different manners such that they are evaluated based on product-specific evidence rather than as a category or class of similar products. **Products with medically necessary uses, based on credible scientific evidence and other relevant factors, are addressed in a related document: CG-SURG-127 Products for Wound Healing and Soft Tissue Grafting: Medically Necessary Uses**.

Unlike products approved through the Premarket Approval (PMA) process or authorized under the 510(k) process which are assigned specific indications for use by the U.S. Food and Drug Administration (FDA), there are no authorized indications for products regulated through the FDA Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P) process as human tissue for transplantation. Use of HCT/P products is therefore guided by

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the available peer reviewed medical literature among other factors, including information provided by manufacturers about proposed uses of the product when HCPCS codes are issued. Additionally, some products may be granted marketing based on alternative FDA pathways, for example De Novo approval, however, no review or submission of data regarding safety or efficacy is required in this process.

Wound care should be well documented and include objective measurements of wound size and depth before, during, and after treatment. Wound measurements should be documented before and after each application of a wound product. Clinical records should describe the planned skin replacement with choice of skin substitute graft/HCTP.

The products listed below are deemed investigational and not medically necessary based on the assessment of relevant FDA information and the published and peer reviewed medical literature summarized. In determining a product's status, credible studies from peer-reviewed journals were evaluated to determine if they materially improve the net health outcome or are as beneficial as established alternatives, among other factors. The products listed in the position statement above and discussed below do not meet these criteria for a variety of reasons. Some products have no published evidence in the peer reviewed medical literature. Many products are supported by evidence limited to case reports or case series. Comparative studies, if available, often lack important methodological considerations, including blinding and randomization, and when these are present, the follow-up duration is typically insufficient to assess the improvement in health outcomes.

The literature discussed and included in this document is considered a summary of notable findings and should not be construed to represent the entirety of scientific evidence available on a topic or reviewed in document development.

Product Specific Evidence

Ac5 advanced wound system

AC5 Advanced Wound System (Arch Therapeutics, Inc., Framingham, MA) is a synthetic, self-assembling peptide-based wound matrix cleared through the FDA's 510(k) process (K182681). Under the supervision of a health care professional, AC5 Topical Gel is a topical dressing used for the management of partial and full-thickness wounds, such as pressure sores, leg ulcers, diabetic ulcers, and surgical wounds.

In a prospective, single-arm study by Treadwell (2024), 15 individuals (6 men, 9 women; ages 25 to 80) with challenging acute or chronic wounds were recruited. Their wounds had a mean duration of 21 months (the oldest at 7 years) and a mean surface area of 9.5 cm^2 (the largest at 32 cm^2). Eleven individuals received weekly AC5 applications, and four received AC5 treatment every other week, for up to 8 weeks. Among the weekly group, 64% achieved more than 50% wound area reduction at 4 weeks, and 73% had more than 60% reduction at 8 weeks. In the every-other-week group, 25% reached 50% reduction by 4 weeks, and 50% by 8 weeks. No adverse events were reported. The authors reported that AC5 easily conformed to uneven wound geometry, including tunneled or undermined wounds. They concluded that the weekly application of AC5 appeared more effective compared to biweekly application.

Aesten Inject (see MegaDerm)

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Affinity

Affinity is a cryopreserved human amnion-derived tissue allograft and is treated as human tissue for transplantation under the FDA's HCT/P process.

Serena (2020) reported on the results of an unblinded prospective RCT involving 76 participants with diabetic foot ulcers (DFUs) treated with either Affinity plus standard care (n=38) or standard care alone (n=38). Wound closure for the Affinity group was significantly greater than that of the control group at both 12 weeks (55% vs. 29%, p=0.02) and 16 weeks (58% vs. 29%, p=0.01). At 16 weeks, wound closure was reported in 60% of Affinity participants vs. 48% of control participants (p=0.04). The authors reported that the probability of wound closure with Affinity vs. standard care increased by 75% (hazard ratio [HR], 1.75). The authors concluded that the use of Affinity increased the frequency and probability of DFU wound closure. Additional data from well-designed trials are warranted to support these conclusions.

AlloMax

AlloMax is an acellular, non-cross-linked allograft dermis product and is treated as human tissue for transplantation under the FDA's HCT/P process.

A case series study involving 65 participants undergoing tissue expander breast reconstruction was described by Venturi (2013). The results of this study are limited but include a complication rate of 4.6% (3 participants). These included one case of cellulitis and two cases of partial mastectomy flap necrosis requiring debridement. No seromas or explantations were reported. Histological verification of full graft incorporation was demonstrated in the first 20 biopsies.

A second retrospective case series involving 203 participants (348 breasts) undergoing mastectomy with immediate breast reconstruction was reported by Rundell in 2014. The authors reported that infection occurred in 6.6% of participants, with 3.7% being major infections requiring intravenous antibiotics and 2.9% being minor infections requiring oral antibiotics only. Seromas occurred in 3.4% of cases and reconstruction failure occurred in 0.6% of cases. The authors stated that the analysis suggested that the complication prevalence was significantly higher in individuals with a BMI > 30 (p=0.03).

AlloPatch

AlloPatch is a product composed of acellular human dermis treated as human tissue for transplantation under the FDA's HCT/P process.

At this time, there is limited evidence published in the peer-reviewed literature addressing the use of this product. The most rigorous study to date involved 45 participants with chronic refractory DFUs (Zelen, 2016b). A total of 40 participants in this investigator blinded randomized controlled trial (RCT) were assigned in a 1:1 fashion to either standard care alone (n=20) or AlloPatch plus standard care (n=20). AlloPatch grafts were applied weekly for up to 12 weeks. Initial ulcer size at baseline was greater in the AlloPatch group compared to controls (4.7 cm^2 vs. 2.7 cm^2). At 6 weeks, the authors reported that 65% of the AlloPatch group participants were completely healed (13/20) compared to 5% in the control group (1/20). At 12 weeks, the proportions of DFUs healed were 80% and 20%, respectively. The mean time to heal within 12 weeks was 40 days in the AlloPatch group compared to 77 days

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for controls. No differences between groups were reported with regard to adverse or serious adverse events. The authors reported that, "Weekly application of HR-ADM [human reticular acellular dermis matrix] is an effective intervention for promoting closure of non-healing DFUs."

This group published a continuation study with an additional 40 participants (n=20 per group) and results of the total 80 participant population were reported by Zelen in 2018. In the continuation population, the AlloPatch group had more smokers (7 vs. 1, p=0.044) and the control group was older (67 years vs. 55 years, p=0.008). At 6 weeks, 85% of the AlloPatch group compared to15% of the controls were completely healed ($p=2.7 \times 10^{-6}$). The mean PAR in wounds was greater in the AlloPatch group (62% vs. 50%, $p=2.7 \times 10^{-6}$). Mean time to healing at the 6-week time point was 27 days for the AlloPatch group compared to 41 days for controls ($p=9.9 \times 10^{-7}$). At 6 weeks, 2 AlloPatch participants (5%) and 19 control participants (48%) were withdrawn from the study due to failure to have a 50% reduction in wound area. At 12 weeks, 80% of AlloPatch participants and 30% of the control participants had complete wound healing ($p=8.4 \text{ X } 10^{-6}$). At 12 weeks, mean time to heal was 38 days in the AlloPatch group compared to 72 days in the control group ($p=3.9 \times 10^{-7}$). After adjusting for age and baseline wound area, the HR for the AlloPatch compared to the control group was 8 ($p=3.7 \times 10^{-7}$). No adverse events related to the study treatment were reported.

AMNIOEXCEL

AMNIOEXCEL is a dehydrated human amnion-derived tissue allograft and is treated as human tissue for transplantation under the FDA's HCT/P process.

Snyder (2016) reported on the results of a prospective, open label, randomized, parallel group trial involving 29 adults with type 1 or type 2 diabetes mellitus who have one or more ulcers presenting for more than 1 month with no signs of infection/osteomyelitis. Participants were randomized in a 1:1 fashion to receive treatment with either standard care (SOC, n=14) or AMNIOEXCEL plus SOC (n=15) until wound closure or 6 weeks. The authors reported that 35% of participants in the experimental group achieved complete wound closure at or before week 6 compared to 0% in the SOC group (p=0.017). They observed that there was a more robust response noted in the per protocol population, with 45.5% of participants in the experimental group achieving complete wound closure, while 0% of SOC alone participants achieved complete closure (p=0.0083).

Amniofix

Amniofix is a product that consists of an injectable form of processed allogeneic amniotic tissue and is treated as human tissue for transplantation under the FDA's HCT/P process.

Zelen (2013b) report on 45 participants with plantar fasciitis randomized in a single-blind fashion to receive one of three treatments: (1) standard care plus injection with 1.25 cc of sterile 0.9% saline (control group); (2) standard care plus injection with 0.5 cc Amniofix (0.5 cc group), and (3) standard care plus injection with 1.25 cc Amniofix (1.25 cc group). All participants also received injection with 2 cc of 0.5% Marcaine plain, and the use of tramadol for pain was allowed as needed throughout the study. There were 15 participants in each group. A total of 41 participants (91.1%) completed the 8-week follow-up period. All 4 participants who failed to complete the study were in the control group. The authors report that significant benefits were seen in all groups throughout the study compared to baseline on the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot Scale ($p<0.01$). Additionally, the AOFAS scale outcomes were significantly higher for both Amniofix groups compared to controls

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(p<0.001). No differences were noted between the two Amniofix groups. At the end of week 1, the median reduction in pain was 3 points for controls and 6 points and 5 points for those receiving 0.5 cc and 1.25 cc of Amniofix, respectively (p<0.001; p=0.004). Using the Wong–Baker FACES Pain Rating Scale, a visual analog pain scale (VAS), controls reported moderate to severe pain throughout the 8-week study period. Both Amniofix groups reported a significant reduction of pain from very severe at baseline to within the mild to moderate range at 1 week and reported continuing reduction in pain over the study period (p<0.001), with no statistically significant difference between groups. Based upon the physical and mental scales on the SF-36v2 quality of life tool, it was reported that both Amniofix groups had significant improvements from baseline compared to controls. No difference between Amniofix groups was reported. At the end of the first follow-up week, significantly more participants in both Amniofix groups compared to controls needed additional treatment with tramadol (57.1% of controls, 73.3% of the 0.5 cc group, and 100% of the 1.25 cc group). This was not significant for the 0.5 cc group compared to controls but was for the 1.25 cc group compared to controls (p=0.004) as well as the 1.25 cc group compared to the 0.5 cc group (p=0.032). At the second follow-up visit, rates of tramadol use were significantly lower in all groups (p>0.05 for all groups). No adverse events related to treatment were observed in any study participants. This study indicates some benefit from the use of Amniofix for individuals with plantar fasciitis. However, due to the small study population and lack of investigator blinding, further research is warranted to fully understand the efficacy of this treatment method.

Amniotic Allografts – Not specified

There is an increasing body of evidence in the available peer-reviewed published literature addressing the use of allogeneic amniotic tissues for the treatment of a variety of uses, including ophthalmologic, obstetric, and burn conditions. A small number of these publications address branded products, which are addressed elsewhere in this document. However, the vast majority of the published studies involve the use of amniotic-derived products that are: (1) not specified by the authors, (2) branded products not commercially available in the U.S, or (3) materials that are locally sourced. Many of these studies are randomized controlled trials, but with small study populations (Abdulhalim, 2015; Amer, 2010; Andonovska, 2008; de Farias, 2016; Harvinder, 2005; Küçükerdönmez, 2007; Luanratanakorn, 2006; Paris, 2013; Sharma, 2016; Sheha, 2008; Tamhane, 2005; Tandon, 2011). These studies are heterogenous with regard to the type of amniotic graft used, including lyophilized, cryopreserved and glycerin preserved products. Furthermore, there is a wide array of indications addressed across these studies, with a critical mass of evidence not established for any particular one. Finally, due to the differences in the harvesting and processing procedures these materials undergo that may impact the physical properties of the materials, the findings of such studies cannot be used to support the use of amniotic-derived products as a group.

Artacent Wound

Artacent is a product composed of dehydrated acellular human amniotic membrane and is treated as human tissue for transplantation under the FDA's HCT/P process.

Sledge (2020) reported on a study involving 26 participants who were participants in an RCT that was discontinued due to logistical issues. All participants had non-infected DFUs that had failed previous standard care and were treated weekly or biweekly with Artacent Wound. The primary endpoint of 100% healing at 12 weeks was reported in 17 participants (65%). The incidence of adverse events potentially related to the grafting product was 12% (4/34) and serious adverse events were reported in 6% (2/34).

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Artelon Tissue Reinforcement (Including CMC and TMC)

Artelon Tissue Reinforcement (Artelon, Inc., Marietta, GA) is a synthetic grafting material made from degradable polyurethaneurea which provides a scaffold that is incorporated into the individual's native tissue. It is intended for use in general surgical procedures for the reinforcement of soft tissue where weakness exists, as well as for reinforcement of soft tissues that are repaired by suture or suture anchors, during tendon repair surgery including reinforcement of rotator cuff, patellar, Achilles, biceps, or quadriceps tendons. Artelon is not intended to replace normal body structure or provide the full mechanical strength to support the rotator cuff, patellar, Achilles, biceps, or quadriceps tendons. Sutures, used to repair the tear, and sutures or bone anchors, used to attach the tissue to the bone, provide mechanical strength for the tendon repair. Artelon is cleared through the FDA's 510(k) process (K071887).

Nilsson, (2010) published the results of an RCT consisting of 109 participants with osteoarthritis of the carpometacarpal joint of the thumb. In this study, 72 participants were treated with Artelon and 37 were treated with standard tendon interposition arthroplasty. There was a significant loss to follow-up, with less than 50% of participants having available data at the 1-year follow-up time point. The authors report that swelling and pain were more common in the Artelon group, and 6 implants were removed because of such symptoms. Interestingly, 5 of these participants did not receive antibiotics preoperatively according to the study protocol. In the intention-to-treat analysis but not in the per-protocol analysis, significantly better pain relief (VAS) was obtained in the control group. Self-perceived disability evaluated by the DASH (disability of arm-shoulder-hand) questionnaire improved in both groups. However, these findings are not particularly useful, given the significant loss to follow-up reported.

At this time, the available peer-reviewed published articles addressing Artelon TMC are case series studies involving 13 and 15 participants each (Jörheim, 2009; Nilsson, 2005; respectively). This level of evidence is inadequate to fully evaluate the safety and efficacy of this product. Further investigation is warranted.

Cuttica (2023) reported the results of a retrospective case series study involving 18 participants undergoing surgical treatment for insertional Achilles tendinosis with tendon repair augmentation using Artelon. The study reported on pain score, strength, and ankle motion. The Wilcoxon signed-rank test was used to compare baseline and final follow-up VAS scores. One participant had 2 suture anchor pull-out from the calcaneus. Final strength was obtained for 17 participants, with 15 (83.24%) reported as being 5/5 and 2 (11.76%) being 4/5. Final active dorsiflexion was measured in all participants, with 17 (94.44%) reaching at least 10°. No participants had evidence of foreign body reaction or neritic complications, required return to the operating room, developed deep vein thromboses, or developed other major complications. The authors concluded that Achilles tendon augmentation with Artelon is a viable option in the treatment and that its use has minimal morbidity and can be an alternative to other forms of augmentation.

ARTIA Reconstructive Tissue Matrix

ARTIA reconstructive tissue mesh (Allergan Inc. Dublin, Ireland) is a product derived from porcine acellular dermal matrix (ADM). ARTIA is intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes which require the use of reinforcing or bridging material to obtain the desired surgical outcome. The implant is intended for reinforcement in plastic and reconstructive surgery. It is intended for single patient; one time use only. ARTIA is cleared through the FDA's 510(k) process (K162752).

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King (2023) reported a retrospective non-randomized comparative trial involving the use of ARTIA for implant-based breast reconstruction in 63 participants compared to 181 participants who received treatment with AlloDerm ADM. Bilateral procedures were done in 95 participants for a total of 276 breasts (n=98 ARTIA and n=178 AlloDerm). Significantly more participants in the ARTIA group received prepectoral reconstruction (69.4% vs. 46.6%, p<0.01). Eleven underwent delayed reconstruction, while 265 underwent immediate reconstruction, with no significant difference between groups (p=0.34). Two stage reconstruction with tissue expanders was utilized in the majority of cases (243 breasts), with no difference in reconstruction technique between groups (p=0.2). The authors reported no significant differences between groups with regards to major complications (28.6% vs 31.2%, p=0.69) or minor complications (9.1% vs 14.0%, p=0.24), including hematoma, infection, seroma, dehiscence, necrosis, capsular contracture, and explantation. The results of this study appear to indicate equivalent outcomes between ARTIA and the standard of care product. However, the small sample size and other methodological issues impair the generalizability if these findings. Further investigation with more robust trials is warranted to establish the clinical utility of this product.

Avance Nerve Graft

Avance Nerve Graft is a decellularized allogeneic product derived from donated peripheral nerve tissue and is treated as human tissue for transplantation under the FDA's HCT/P process.

A comparative trial involving this product was published by Means in 2016. This double-blind RCT involved 23 participants with 31 digital nerve injuries treated with hollow conduit (n=9) or Avance processed nerve allograft (PNA) (n=14). The authors reported that the Avance group demonstrated significantly greater recovery compared to conduit participants as measured by results by static 2-point discrimination (5 ± 1 mm vs. 8 ± 5 mm, p<0.5). Among participants with 6-month data available, all participants in the Avance group returned to S3+ (8 of 8 digits) compared to 75% (9 of 12 digits) in the conduit group. A return to S4 was not statistically significant between groups. At 12 months, results of Semmes-Weinstein Monofilament (SWMF) assessment testing found that the Avance group had a significant improvement compared to controls (mean of 3.6 ± 0.7 vs. 4.4 ± 1.4, p<0.05) and recovery of protective sensation, equivalent to SWMF score of 4.31 or better, was reported in 100% of Avance-treated participants compared to 75% of control participants. No differences between groups were found with regard to results on the Disability of the Arm, Shoulder and Hand (DASH) questionnaire or assessment of thermal discretion or pain assessment at 12 months. While this study had a rigorous methodology, the small numbers of participants and significant loss to follow-up (> 70%) hinder the utility of the results.

Brooks and others (2011) reported a case series study involving 108 participants with nerve injuries. Outcomes were only available for 59 participants (56%). The authors report "meaningful recovery" in 87% of participants available for evaluation. A post hoc subgroup analysis demonstrated no significant differences with regard to nerve type, gap length, participant age, time to repair, age of injury, or mechanism of injury (p>0.05). No graft-related adverse experiences were reported and a 5% revision rate was observed. The data presented is insufficient to allow full assessment of the safety and efficacy of the Avance nerve graft.

Safa (2019) reported a case series study involving data from the RANGER® registry involving 385 participants who underwent 624 nerve repair procedures using Avance and were compared to historical data from participants undergoing hollow tube conduit and/or autografts. Follow-up was 12 months for sensory nerves and 18 months for mixed/motor nerves. Overall response rate was reported to be 87%, with response being defined as "any

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improvement after repair based on either qualitative and/or quantitative assessments". Meaningful recovery, defined as S3 or M3 or greater improvement as measured by the Mackinnon-Dellon Modification of the Medical Research Council Classification (MRCC) sensory and motor scale, was reported as 82% of participants. By body region, meaningful recovery was reported as 83%, 53% and 100% for the upper and lower extremity and head/neck, respectively. The difference between upper and lower extremity was significantly different (n=0.01). Compared to historical comparisons, the author's findings were not significantly different. For upper extremities, nerve gap lengths < 15 mm had significantly better meaningful recovery than those 50-70 mm (p=0.011). No differences in meaningful recovery stratified by gap length were reported for the lower extremities.

Ilyas (2024) reported a multicenter US based RCT that included 220 participants with digital nerve injuries treated either with type I bovine collagen conduit (CONDUIT) or a PNA. The CONDUIT group used the NeuraGen Nerve Guide, the PNA group used the Avance Nerve Graft. Inclusion criteria was individuals 18- to 69-years with 5 to 25 mm digital nerve gaps within 24 weeks of injury. Participants were randomized (1:1) to PNA or CONDUIT repairs. Cold Intolerance Symptom Severity (CISS) scores and sensory function testers were assessed at first visit (FPV), 1-, 3-, 6-, 9-, and 12-months post-surgery, both participants and assessors were blinded to treatment. A total of 183 participants completed the last evaluable visit (LEV) of 6 months or more of follow-up. Of these, 91 received PNA repair and 92 had CONDUIT repair. No significant differences were observed in demographics, gap length, time to repair, or injury mechanism between the groups. The average gap lengths were 13.6 mm for the PNA group and 13.0 mm for the CONDUIT group. The average time to repair was 28.2 and 23.4 days, respectively. Both groups reported a reduction in the CISS over time, indicative of improved cold intolerance symptoms. The mean CISS score for the entire cohort decreased from 31.15 ± 29.25 at FPV to 23.42 ± 22.16 at the LEV. The reduction in CISS score was numerically greater but not statistically different in the PNA group (10.39 points) compared with the CONDUIT group (5.23 points). A sub-analysis showed more participants improved from severe/extremely severe cold intolerance to mild cold intolerance for PNA compared with CONDUIT at 1 month and LEV ($p<0.05$). The CISS scores also correlated with sensory function testing. The authors concluded that PNA had improved cold tolerance outcomes for participants with more severe cold intolerance at FPV relative to nerves repaired with CONDUIT. Study limitations include the loss to follow-up at later timepoints in the study; at the 1-month timepoint, the study had a total of 178 participants, but by 12 months, only 149 were available for evaluation. Target follow-up for the study was 12 months; however, participants were assessed at or greater than 6 months, which included up to 15 months out from repair. The study did not include a sub-analysis of participants who concomitantly underwent vascular repair. This was due to a low overall number of participants with vascular injury requiring repair, which is likely a result of the exclusion criteria of the study as well as study design limitations. This limits the generalizability of this study to individuals with nerve injuries who do not require vascular repair.

Avaulta

Avaulta (C.R. Bard, Inc., Murray Hill, New Jersey) is a composite product composed of polypropylene mesh with acellular cross-linked collagen of bovine origin. Avaulta Plus and Avaulta Biosynthetic Support System are indicated for tissue reinforcement and long-lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended either as mechanical support or bridging material for the fascial defect. Avaulta is cleared through the FDA's 510(k) process (K063712).

The use of Avaulta Plus and Avaulta Biosynthetic Support System for the treatment of vaginal prolapse has been described in one prospective case series study involving 40 participants (Bondili, 2012). Participants were followed for up to 3 years (median 27 months (range 20-36). The primary outcome was quality of life (QoL) and satisfaction

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as measured by the International Consultation on Incontinence Modular Questionnaire–Vaginal Symptoms (ICIQ-VS) tool. Twelve participants (30%) were undergoing a second procedure to address prolapse. Of the 40 participants, 19 (47%) underwent anterior repair, 20 (5%) posterior repair, and 1 (2.5%) underwent both anterior and posterior procedures. Vaginal laxness improved significantly, with 67.25% of participants reporting preoperative laxness which improved to 5% of participants with laxness at follow-up ($p<0.0001$). Decreased vaginal sensation also improved, from 30% to 7.5% ($p<0.01$). Sexual activity was reported to improve from only 32% to 100% postoperatively. The authors report that 1 participant continued to have prolapse symptoms (2.5%), resulting in a 97.5% success rate ($p<0.0025$). Only 2 participants (5%) needed to digitate the vagina to vacate their bowels, a significant decrease from 12 (57%) preoperatively ($p<0.001$). Vaginal pain decreased from 55% preoperatively to 2.5% postoperatively ($p<0.0001$). No surgical complications were mentioned.

A retrospective case series study by Oliveira (2020) involved 97 participants with ≥ stage II genital wall prolapse repair with Avaulta. Mean follow-up was 2.9 years with 12 participants lost. Postoperative complications were experienced by 29.1% (n=23) of participants, with one removal due to hematoma. Other complications included voiding dysfunction (n=10), urinary infection (n=7), vesicovaginal fistula (n=1), pelvic abscess linked to hysterectomy (n=2), and mesh exposure (n=6). For participants with voiding dysfunction and bladder injury, a prolonged bladder drainage by a Foley catheter was required for a mean duration of 11.2 days. Four of the participants with vaginal mesh exposure required additional surgery to partially remove the mesh in 3 cases and a colpoplasty procedure to cover the mesh in the remaining case. Self-reported improvements were reported with regard to vaginal discomfort (n=79 at baseline vs. 4 at last follow-up, $p>0.01$), pelvic heaviness (n=46 at baseline vs. 3 at last follow-up, $p>0.01$), and voiding dysfunction (n=16 at baseline vs. 2 at last follow-up, $p>0.01$). No anterior wall prolapse was present in 79.1% of participants at last follow-up and stage I and II prolapse was reported in 19% and 3%, respectively. No apical and posterior prolapse was reported in 98.5% and 83.6%, respectively. Eight participants (12 %) had a recurrence at 3 years.

Avive

Avive Soft Tissue Membrane is a product derived from allograft amnion and umbilical cord membrane, which is regulated through the U.S. FDA's HCT/P process as human tissue for transplantation.

Cox (2023) reported the first use of Avive in a prospective propensity-matched cohort study involving 77 participants (97 nerves) who underwent revision nerve decompression. Mean follow-up was 9.0 months. Avive was applied to the median nerve in 47.4% of cases, ulnar nerve in 39.2% of cases, and radial nerve in 13.4% of cases. In the Avive cohort, S4 sensory recovery was achieved in 58% of participants, S3+ in 33%, S3 in 7%, S0 in 2%, and improvement from baseline in 87%, strength was improved in 92%. Mean total active motion was 94.8%. Mean Quick Disability of Arm, Shoulder & Hand (QuickDASH) score was 36.1, and 96% reported improved or resolved symptoms. For between-group comparisons, postoperative pain was significantly lower in Avive group participants ($p=0.001$). Improved or resolved symptoms were more frequently reported in the Avive group ($p<0.0001$). Finally, clinically important improvement in pain was reported in 64.9% in the Avive group compared to 40.8% the control group ($p=0.002$). This initial pilot study indicates some benefit to the use of Avive in revisions nerve surgery. Further investigation is needed to fully understand the benefits and harms of such use.

BEAR (Bridge-Enhanced ACL Repair) Implant

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In December 2020, the FDA granted De Novo (DEN200035) approval of the BEAR Implant (Miach Orthopaedics Inc. Westborough, MA). BEAR is a decellularized xenograft derived from bovine collagen and is indicated for repair of anterior cruciate ligament tear (ACL). The graft implant is combined with autologous whole blood to form a clot that replaces the ACL and functions as a bridge between the torn ends of the ligament.

Murray (2020) and Barnett (2021) both reported the results of the BEAR II trial, a double-blind RCT involving 100 participants aged 13-35 years with a complete midsubstance ACL injury treated with BEAR (n=65) or autograft ACL (n=35). Participants underwent surgery within 45 days of the index injury. Participant outcomes were assessed at 2 years by an independent examiner blinded to the procedure. Murray reported that the results on the International Knee Documentation Committee (IKDC) Subjective Score were 88.9 points for the BEAR group and 84.8 points for the control group (no p-value reported). The side-to-side difference in AP knee laxity in the BEAR group was 1.61 mm compared to 1.77 mm in the control group (no p-values reported). The BEAR group had a significantly higher mean hamstring muscle strength index than the control group at 2 years (98.2% vs. 63.2%; $p<0.001$). The report by Barnett stated that repeated-measures testing revealed a significant effect of group on the IKDC Subjective Score ($p=0.015$), most pronounced at 6 months after surgery (86 points in the BEAR group vs. 78 points in the control group; $p=0.001$). Results on the Knee Injury and Osteoarthritis Outcome Score-Symptoms subscale scores were significantly in favor of the BEAR group ($p=0.010$) attributable to higher BEAR scores at 1 year (88 vs. 82; $p=0.009$). Hamstring strength was significantly better in the BEAR group compared to controls ($p<0.001$). Clearance for return to sports at 1 year after surgery was granted to approximately 88% of BEAR group participants and 76% of control group participants ($p=0.261$). The authors concluded that participants undergoing the BEAR procedure had earlier resolution of symptoms as well as increased satisfaction with knee function and hamstring muscle strength.

Barnett (2020) also compared sex-specific outcomes following ACL reconstruction within 45 days of injury in 65 participants with complete ACL tear treated with BEAR. The results demonstrated no significant sex difference on the postoperative IKDC Subjective Score or any of the five Knee Injury and Osteoarthritis Outcome (KOOS) scores at 12 and 24 months. Additionally, AP laxity testing demonstrated differences that were similar in the two sexes at 2 years (1.7 mm and 1.5 mm in females and males, respectively; $p=0.72$). At 6 months postoperatively, males had a larger deficit in hamstring strength on the operated leg (14.0% vs. 1.7%; $p=0.03$) and a larger deficit in quadriceps strength on the operated leg (11.3% vs. 2.0%; $p=0.004$); however, no differences were noted at 12 or 24 months. Interestingly, females demonstrated superior single leg hop testing at both 6 and 12 months (91.3% vs. 78.1%, $p=0.001$ and 96.9% vs. 87.0%, $p=0.01$, respectively). No significant differences were reported with regard to ipsilateral ACL reinjury rates.

Menghini and others (2022) completed a cohort study using data from the above-mentioned BEAR II trial, examining the cross-sectional area (CSA) of the treated compared to contralateral native ACLs (n=65 in the BEAR group, n=35 in the autograft group, n=100 in the native group). CSA is a known predictor of strength and knee function. The authors reported that at 24 months, CSA in the autologous group peaked at 69%, 61% in the BEAR group, and 42% in the native group, with significant between-group differences ($p<0.001$). They concluded that while the BEAR ACLs remained significantly larger, the autograft ACL had a CSA profile comparable with that of the contralateral native ACL.

Flannery (2023) reported the results of a retrospective analysis of 65 individuals from the BEAR II RCT, that compared BEAR graft to traditional ACL reconstruction using non-contemporaneous quantitative MRI to predict positive functional outcomes from 6-24 months post-ACL surgery. The study images were obtained at 6 months

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post-surgery, additionally single-leg hop test ratios, arthrometric knee laxity values, and IKDC subjective scores were measured at 6 and 24 months. The results demonstrated that CSA (r=0.44, p=0.01), volume (r=0.44, p=0.01), and estimated failure load (r=0.48, p= 0.01) measures at 6 months were predictive of the change in single-leg hop ratio from 6 to 24 months in bivariate analysis. The authors concluded that using qualitative MRI at 6 months post-surgery may be a predictor of longer term functional outcomes. This information may be useful in rehabilitation planning, return to sport decisions, and injury risk reduction.

Current evidence does not yet support that use of BEAR Implant for the treatment of ACL injury is a durable equivalent to standard of care ACL reconstruction.

Belladerm

BellaDerm is a product composed of acellular human dermis and is treated as human tissue for transplantation under the FDA's HCT/P process.

Solomon and others (2013) published the results of a retrospective case series study involving 47 participants who underwent penis girth enhancement utilizing circumferential grafting with allograft material. The participants received either aseptic AlloDerm (n=9), Belladerm (n=20), and Repriza (n=21). Mean follow-up was 11.25 months (range 1 to 120 months). The rate of infection, which the authors defined as an open wound with graft exposure, occurred in 20 (42%) of 47 participants. Of these, 17 (36%) participants had graft exposure only and 3 (6%) participants sustained graft exposure and total graft loss. Graft exposure or loss occurred in 3 AlloDerm participants, 9 Belladerm participants, and 8 Repriza participants. No AlloDerm participants sustained graft loss, whereas 2 with Belladerm and 1 with Repriza did. No statistical differences between groups with regard to infection or graft loss was reported.

BioBrace Implant

BioBrace Implant (CONMED Corp., Largo, FL) is a bioresorbable scaffold made from bovine tendon collagen and reinforced with polyL-lactic-acid (PLLA) yarn. The device is designed for surgical reinforcement of weakened soft tissues it supports tissue healing in surgeries such as tendon repairs, including rotator cuff, patellar, Achilles, biceps, and quadriceps tendons. BioBrace is not intended to replace normal body structures or provide the full mechanical strength to support the rotator cuff, patellar, Achilles, biceps, or quadriceps tendons. Sutures, used to repair the tear, and sutures or bone anchors, used to attach the tissue to the bone, provide mechanical strength for the tendon repair. BioBrace is cleared through the FDA's 510(k) process (K203627).

Biodesign Please see 'Surgisis' section below.

CardioCel

CardioCel (Admedus Inc, Brisbane, Australia) is a product produced from bovine pericardial tissue, it is indicated for use as a patch in pericardial closure and the repair of cardiac and vascular defects including intracardiac defects; septal defects, valve and annulus repair; great vessel reconstruction, peripheral vascular reconstruction and suture line buttressing. CardioCel is cleared through the FDA's 510(k) process (K130872).

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Pavy (2017) published the results of a retrospective series of 102 participants who underwent procedures addressing a variety of congenital heart diseases, including septal defects to pulmonary outflow disorders. No infections, intraoperative implantation difficulties or postoperative mortality were reported to be associated with CardioCel. Graft failure reoperations occurred in 5 participants (5%), 4 of whom had the patch implanted for aortic angioplasty (2 in the ascending aorta and 2 in the aortic arch), and 1 participant had a monocusp replacement. The median time between the first and the second operation for graft failure was 245 (range 5-480) days. The authors concluded that, "Our experience shows that the patch is well tolerated in the septal, valvar and pulmonary artery positions. However, we experienced graft failures in infants in the aortic position."

Bell (2019) reported on the results of another series study involving 377 participants with congenital heart defects who received surgical treatment with 501 CardioCel patches. Median follow-up was 31 months (1-60 months), and 11 deaths (2.9%) were reported, with 1 reportedly related to Cardiocel. The authors reported no echocardiographic or radiological evidence of patch calcification in any participant. The overall freedom from reintervention at 3- and 5-years post-implantation was 96%. A total of 14 (2.8%) implants required 18 reinterventions (3.6%) at the site of implantation. No differences in performance of CardioCel in neonates (0-28 days), infants (29-365 days) or children older than 1 year (p=0.22) were reported. Patukale (2023) reported on the mid-term performance of CardioCel for the repair of congenital heart defects. The retrospective study included a total of 1184 CardioCel patches implanted in 752 pediatric participants. Median age at implant was 12 months with median follow-up of 2.1 years. The authors reported the probability of freedom from CardioCel-related reintervention as 93% at 1 year, 91% at 3 years, and 88% at 5 years, respectively. A multivariable regression analysis indicated that participants undergoing aortic valve repair had a higher incidence of reintervention compared to other sites (HR, 7.15, p=0.008). They also stated that the probability of reintervention was higher in neonates (HR, 6.71, p=0.0007), especially when used for augmentation of the pulmonary arteries (HR, 14.38, p=0.029).

CellerateRX

CellerateRX Surgical Hydrolyzed Collagen Powder (Sanara Med Tech, Fort Worth, TX) is a wound dressing that is derived from bovine collagen. CellerateRX is purported to absorb wound fluid and maintain a moist wound environment, it may be used in the management of partial and full thickness wounds, pressure ulcers (Stage I-IV) and venous ulcers, ulcers caused by mixed vascular etiologies, venous stasis and diabetic ulcers, 1st and 2nd degree burns, cuts, abrasions and surgical wounds. CellerateRX is cleared through the FDA's 510(k) process (K171645).

A retrospective nonrandomized, controlled study by Sultan (2024) involving 76 individuals undergoing spinal fusion with paraspinal flap reconstruction evaluated the use of CellerateRX (n=47) compared to standard care (n=29) . Compared to the standard care group, the CellerateRX group had a higher rate of seroma formation (approximately 28% vs. 7%, p=0.03), but no significant differences in wound dehiscence (p=0.17), hematoma (p=1.0), infection (p=0.58) or reoperation (p=0.58). Additional well-designed research with larger, more diverse populations and longer follow-up is warranted.

Clarix

Clarix is a product composed of cryopreserved acellular human amniotic membrane and umbilical cord and is treated as human tissue for transplantation under the FDA's HCT/P process.

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Bemenderfer (2019) provided the only currently available published peer-reviewed study on this product. The unblinded non-randomized study involved 104 participants undergoing total ankle arthroplasty who received skin closure with either Clarix (n=54) or standard care (n=50). The authors reported that the use of Clarix significantly decreased the overall time to skin healing (28.5 days vs. 40 days; p=0.03). No differences between groups were reported with regard to reoperations, skin dehiscence, local wound care, or antibiotic prescriptions.

Ross (2022) reported a single center, retrospective study of pain outcomes in 52 individuals with musculoskeletal spinal disorders who were treated with ClarixFLO via epidural and facet injections. Conditions treated included; spondylosis (n=44), intervertebral disc (n=31), radiculopathy (n=18), stenosis (n=2), and other conditions. Pain was rated by participants on a scale of 0-10 where 0 indicated no pain and 10 indicated the worst imaginable pain. The average baseline pain score was 4.9, the mean duration of symptoms was 54.2 months. After ClarixFLO treatment, pain ratings decreased to 3.4 at 2 weeks ($p<0.0001$) and 3.5 at 3-4 weeks (p=0.0023). During the follow-up period (average 10.6 weeks), pain was reduced to 2.8 ($p<0.0001$) compared to baseline. There were no adverse events reported, and the authors concluded that additional larger studies are needed to confirm the safety and efficacy of ClarixFLO in epidural and facet injections.

Madan (2023) published a study that analyzed the use of ClarixFLO in the treatment of cystitis and bladder pain. In the first study, 5 natal females average age 64.4 (± 20.1 years) who had a median chronic radiation cystitis (CRC) duration of 10 years that was refractory to previous treatment modalities, received amniotic bladder therapy with ClarixFLO. The therapy was comprised of intra-detrusor injections of 100 mg micronized ClarixFLO diluted in 0.9% preservative-free sodium chloride. Outcomes measured were the Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS), Overactive Bladder (OAB) Assessment Tool, and SF-12 Health Survey prior to surgery and 2, 4, 8 and 12 weeks post-injection. After treatment with ClarixFLO the BPIC-SS scores improved from baseline to 12 weeks (36.6 compared to 12.6); this was also associated with an improvement in ICSI, ICPI, OAB, and SF-12 scores. Additionally, uroflow assessments showed increases in voided volumes for all individuals. One individual was diagnosed with an acute urinary tract infection at 2 weeks which was treated successfully with oral antibiotics. No other adverse events were observed. The authors concluded that the results provide proof of the potential benefits of ClarixFLO in treating CRC.

A study by Radoiu (2023) involved 10 natal females aged 47.4 (± 14.4 years) with interstitial cystitis/bladder pain syndrome (IC/BPS) that had been refractory to previous treatment modalities for an average 7.8 years who received intra-detrusor injections of 100 mg ClarixFLO diluted in 0.9% preservative-free sodium chloride. Again, the outcomes measured were the ICSI, ICPI, BPIC-SS, Overactive Bladder Assessment Tool, and the SF-12 Health Survey prior to surgery and 2, 4, 8 and 12 weeks post-operatively. After treatment with ClarixFLO, voiding symptoms and bladder pain improved from pre-injection to 3 months. BPIC-SS decreased from 37.4 at baseline to 12.2 at 3 months ($p<0.001$). There were no adverse events reported. The authors concluded that ClarixFLO may be a treatment option for individuals with IC/BPS symptoms based on the preliminary results.

In a single-center, retrospective case series study by Krystofiak (2024) Clarix Flo was used to treat acute muscle or ligament tears in 10 collegiate athletes. The authors reported an average return to play of nearly 30 days, with no complications observed. These preliminary results suggest potential to expedite recovery with Clarix Flo, but additional high-quality investigations with larger, more diverse populations and longer follow-up are warranted.

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A controlled retrospective study involving 113 individuals undergoing meniscectomy was reported by Duru (2024). Treatment with platelet rich plasma was done in 40 participants, treatment with Clarifix Flo in 24 participants, and no adjunctive therapy was done in 49 participants. The authors reported significant differences at baseline between the groups with regard to sex, age, and International Cartilage Repair Society (ICRS) classification grade ($p<0.05$). The average VAS pain severity was significantly decreased only in the Clarifix Flo group at 6 months, compared to baseline ($p=0.0143$), but not at 12 months ($p=0.12$). No significant differences in pain severity of frequency were noted in the platelet rich plasma or no adjunctive therapy groups through 12 months. At 12 months. No differences between groups were reported with regard to Lysholm Knee Scoring Scale, IKDC Subjective Knee Evaluation Form Scores or overall, Knee Injury and Osteoarthritis Outcome Score results. The Clarifix Flo group did demonstrate a reduced reoperation rate (8.3%) compared to the platelet-rich plasma (30%) and no adjunctive therapy groups (40.8%, no p-values provided). However, the single-center design, retrospective methodology, and relatively short follow-up limit the conclusiveness of these findings. While these results indicate some potential benefit, additional high-quality trials with larger, more diverse cohorts and longer follow-up are necessary.

CorMatrix

CorMatrix (CorMatrix Cardiovascular Inc., Roswell, Georgia) is an extracellular matrix scaffold produced from acellular porcine small intestinal submucosa. The CorMatrix suite of products are cleared through the FDA's 510(k) process; including CorMatrix Patch for Cardiac Tissue Repair which is intended for use as an intracardiac patch or pledget for tissue repair (i.e., atrial septal defect (ASD), ventricular septal defect (VSD), etc.) and suture-line buttressing (K063349) and CorMatrix ECM for Vascular Repair which is intended for use as a patch material for repair and reconstruction of peripheral vasculature including the carotid, renal, iliac, femoral, and tibial blood vessels which may be used for patch closure of vessels, as a pledget, or for suture line buttressing when repairing peripheral vessels (K140789).

At this time, there is very limited peer-reviewed published evidence addressing the use of CorMatrix. The data that is available addresses its use in cardiovascular surgical procedures. The largest of these studies is a retrospective, nonrandomized control study involving 111 participants undergoing coronary artery bypass surgery (CABG) who had pericardial reconstruction with CorMatrix, compared to 111 control participants who underwent a standard CABG procedure without pericardial reconstruction (Boyd, 2010). The authors reported that postoperative atrial fibrillation occurred in 39% of controls compared to 18% of CorMatrix participants. No other results were significantly different. The safety and value of CorMatrix is difficult to interpret in this study, as it is the pericardial reconstruction procedure that seems to be the significant variable. Another publication by Quarti (2011) describes the use of CorMatrix in a wide variety of cardiovascular surgeries, with no comparison groups provided. While the authors report no significant complications due to the use of CorMatrix, this study provides little in the way of helpful data to determine the safety and efficacy of this product. Similarly, Kelley and others (2017) reported the results of a retrospective case series study of 25 participants who underwent anterior leaflet augmentation. They reported a 32% recurrence rate of mitral regurgitation and concluded that further research is needed. Finally, Ashfaq (2017) reported good results from the use of CorMatrix in a case series of 15 pediatric participants undergoing atrioventricular (AV) septal defect repair. They reported 12 (80%) participants either improved or had stable left AV valve performance remaining at "mild" or less insufficiency, two (13%) declined from "none" to mild, and one (7%) from declined from mild to "severe," No residual shunting or left ventricular outflow tract (LVOT) obstruction was noted at follow-up. Only one (7%) reoperation was performed after 3 years due to left AV valve zone of apposition dehiscence. No permanent pacemakers were needed, and no deaths were reported.

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Hu and others (2021) reported the results of a retrospective cohort study of 38 pediatric participants undergoing aortic valve repair with the aortic cusp extension procedures with either autologous pericardium (n=30) or CorMatrix (n=8). The authors reported that for the entire cohort the peak trans-valvular gradient significantly decreased immediately postoperatively (p=0.0017). No significant changes were observed at the 5-year follow-up timepoint (p=0.36). In the autologous group participants with aortic stenosis at baseline the peak trans-valvular gradient did not significantly change at follow-up (p=0.12). The CorMatrix group had only 4 participants with aortic stenosis at baseline, which did not allow for sufficient data for between-group tests. Moderate-to-severe aortic regurgitation was reported in 28 (93%) of autologous group participants at baseline, which improved to 11 (37%) postoperatively, but increased to 21 (70%) at follow-up. Eight (100%) CorMatrix group participants had moderate-to-severe aortic regurgitation, which improved to 3 (38%) postoperatively and increased to 7 (88%) at time of follow-up. Between-group data indicated a significant difference in favor of the autologous group (p=0.017). Freedom from reoperation at 5 years was significantly poorer in the CorMatrix group (12.5%) compared to the autologous group (62.5%, p=0.01). The most common reason for reoperation in the autologous group was for repair of moderate to severe aortic regurgitation and severe aortic regurgitation in the CorMatrix participants. While no CorMatrix participants had severe aortic regurgitation postoperatively, 88% developed it at 5 years follow-up. The authors concluded that autologous pericardium may outperform CorMatrix for aortic valve repair using the cusp extension method. However, several methodological weaknesses of this study limit the generalizability of these findings and further study is warranted.

Cymetra

Cymetra, an injectable micronized particulate form of aseptic AlloDerm (decellularized human dermis), has been proposed as a minimally invasive tissue graft product. It is treated as human tissue for transplantation under the FDA's HCT/P process.

Morgan (2007) published a retrospective, nonrandomized controlled trial involving 19 participants undergoing injection laryngoplasty with Cymetra or medialization laryngoplasty. The authors reported no significant difference between groups at 3 months follow-up. No long-term comparison data was provided. Another report of a retrospective case series study involving 10 participants who all received injection laryngoplasty was reported by Milstein et al (2005). The authors of this study reported significant improvement in voice quality, glottal closure, and vocal fold bowing. Of the study population, only 8 participants (40%) were found to have lasting benefit. Finally, Karpenko and others (2003) reported the results of a case series study (n=10). The results indicated that there were no significant quantitative or subjective voice quality improvements. They also stated that significant improvements were identified in maximum phonation time, relative glottal area, and subjective judgment of glottal competency. However, these results were not maintained at the 3-month study interval.

Cytal

Cytal Wound Matrix (ACell Inc., Columbia, MD) is composed of porcine-derived extracellular matrix scaffolds, specifically known as urinary bladder matrix. Cytal Wound Matrix is intended for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunnel/undermined wounds, surgical wounds (donor sites/ grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears), and draining wounds. The device is intended for one-time use. Cytal is cleared through the FDA's 510(k) process (K152721).

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Huen (2022) published a retrospective case series study involving 10 pediatric participants undergoing corporal graft and correction of ventral curvature in proximal hypospadias repair. Median follow up was 14.1 months. Mean ventral curvature after degloving was 80 ± 50 degrees. All participants had straight erections at baseline and 9 had straight erections verified at a subsequent artificial erection test at least 6 months from the corporoplasty (90%). The remaining participant underwent a further procedure and had straight erections per parental history. No participants developed corporal diverticulum or demonstrated induration at site of corporoplasty on physical exam. There were no parental reports of atypical adverse systemic effects. This unique use of a graft product may provide some clinical benefit. However, the clinical utility should be established in larger, more robust trials.

Dermacyte Amniotic Wound Matrix

Dermacyte (Merakris Therapeutics, Triangle Park, NC) is an amniotic membrane allograft regulated by the FDA under HCT/P process as human tissue for transplantation.

Ditmars (2024) described the results of a multicenter retrospective trial involving 11 individuals with a total of 18 refractory diabetic or venous leg ulcers with Dermacyte. Ulcer volumes decreased by about 34% after the first application ($p<0.005$; 95% confidence interval [CI], –0.5319 to –0.1790), and most ulcers reached a 50% reduction in size after about three applications ($p<0.0001$). Both ulcer types showed rapid improvement, although healing trajectories varied, especially among "rapid responders." While these findings appear promising, the small study population, short follow-up period, further high-quality research with larger, more diverse cohorts is warranted.

Derma-Gide

Geistlich Derma-Gide (Geistlich Pharma, Princeton, NJ) is an acellular porcine collagen xenograft sheet. The product is designed to manage wounds, including partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, surgical wounds (donor sites/grafts, post Moh's surgery, post laser surgery, podiatric, wound dehiscence), and traumatic skin wounds (abrasions, laceration, second degree burns, skin tears). Geistlich Derma-Gide is cleared through the FDA's 510(k) process (K182838).

Derma-Gide was the subject of a 2024 multicenter prospective, parallel-group RCT comparing its efficacy to standard of care (SOC) for treating full-thickness, non-infected, non-ischemic diabetic foot ulcers (DFUs) (Armstrong, 2024). SOC consisted of a moisture-retentive, conformable collagen alginate dressing. The study included 105 participants who were randomized to either treatment groups (n=54 purified reconstituted bilayer membrane (PRBM); n=51 SOC) in the intent to treat (ITT) group and 80 who completed the study per protocol (PP) (n=47 PRBM; n=33 SOC). The primary endpoint was the percentage of wounds closed after 12 weeks. Secondary outcomes included percent area reduction, time to healing and quality of life. The proportion of wounds healed at 12 weeks in the PRBM was 83% compared to 45% for SOC, p=0.00004. The time to heal within 12 weeks was shorter in the PRBM group, 42 days compared to 62 in SOC, p=0.005. The PAR values at 12 weeks was a mean of 93.6 for the PRBM participants compared to 50.5 for SOC. The DFUs treated with PRBM healed at a higher rate than those treated with SOC (ITT: 83% vs. 45%, , PP: 92% vs. 67%, p=0.005). Wounds treated with PRBM also healed faster than those treated with SOC; mean of 42 versus 62 days for SOC (p=0.00074) and mean wound area reduction within 12 weeks of 94% versus 51% for SOC (p=0.0023). In the SOC group, 17 participants were withdrawn or lost to follow-up. A total of 14 were withdrawn due to the index ulcer presenting a PAR <50% at week 6, while one participants ulcer was reopened at the healing confirmation visit. Additionally, two

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participants were removed due to adverse events, but there was reportedly no causal relationship between the adverse events and the treatment.

DermaPure

DermaPure is an acellularized human skin-derived product regulated through the FDA's HCT/P process as human tissue for transplantation.

In a retrospective case series by Corlee (2024) of 42 participants diagnosed with insertional Achilles tendinopathy, individuals underwent partial detachment of the Achilles tendon, excision of the retrocalcaneal exostosis, thorough debridement, and repair augmented with DermaPure without suture anchor reattachment. Over a mean follow-up of 20.8 months, the average visual analog scale score improved from 5.1 to 1.9, and participants achieved weight-bearing at an average of 4.4 weeks. Of the 42 participants, 11 (26.2%) experienced complications, including a single rupture (2.4%) in the early postoperative period. No infections were reported, and 4 participants (9.5%) required reoperation. The authors suggest that these findings indicate acellular dermal matrix augmentation without anchor fixation can offer satisfactory outcomes and may justify further investigation under controlled, comparative designs.

DuraGen

DuraGen (Integra Lifesciences Corp. Plainsboro, N.J.) is an absorbable implant for the repair of dura mater, it is a suture less onlay graft comprised of a porous, highly purified collagen matrix and a thin layer of hydroxypropyl methyl cellulose (HfPMC). DuraGen is indicated as a dura substitute for the repair of dura mater. The graft is a porous scaffold that is purported to promote rapid fibrin clot formation while promoting natural dural growth, it contours to surfaces of the brain and spinal cord forming a biological seal to protect against CSF leakage. DuraGen is cleared through the FDA's 510(k) process (K120600).

Hamrick (2023) performed a retrospective, single-center study of 106 individuals who had Chiari decompression surgery by a single surgeon. The study compared the incidence of graft-related complications after posterior fossa surgery using AlloDerm alone compared to AlloDerm with a DuraGen underlay. The inclusion criteria were ≥ 18 years of age, radiographic and clinical findings of Chiari 1 malformation. The exclusion criteria were individuals younger than 18 years, had a previous Chiari decompression, or had Chiari type 2 with associated spina bifida. The AlloDerm-only group had a percutaneous cerebrospinal fluid (CSF) leak rate of 8.6% versus a 0% rate in the dual graft group (p=0.037). At initial follow-up, there was a 15.5% combined rate of pseudomeningocele formation plus CSF leak in the AlloDerm-only group, and 18.8% in the AlloDerm plus DuraGen group (p=0.659). However, the pseudomeningoceles were larger in the AlloDerm-only group (p=0.004) and 5 individuals in the group required surgical repair (56%). All pseudomeningoceles resolved without the need for surgery in the AlloDerm plus DuraGen group (p=0.003). The authors concluded that DuraGen underlay with a sutured AlloDerm dural patch resulted in fewer CSF-related complications and eliminated the need for reoperation compared with AlloDerm alone. This single-center study provides promising evidence that dural grafts with a DuraGen may decrease the risk of complications, however larger RCT's are needed to analyze the efficacy of DuraGen in reducing rates of postoperative pseudomeningoceles and cerebrospinal fluid leak following Chiari decompression surgery.

Xu (2023) completed a retrospective case series review of 1011 individuals who had an open surgical procedure for microvascular decompression using a retrosigmoid approach. The study objective was to identify factors that may lead to CSF leak after a microvascular decompression procedure. Of the individuals who had the procedure, 37

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(3.7%) presented with postoperative CSF leaks. Individuals with and without CSF leaks were not statistically different in age, sex, BMI, diagnoses, prior treatment, or comorbidities. In both groups most individuals presented with Type I trigeminal neuralgia. The results demonstrated that CSF leak after a craniotomy occurred more frequently compared with a craniectomy (13.5% compared to 3.0%), p=0.001. Individuals were more likely to develop a CSF leak with closure of air cells with bone wax, (p=0.002) and compared to the use of Cranios/Norian bone cement, (p=0.01), CSF leak rates were higher with the use of both Durepair (dural substitute) or DuraGen (dural onlay), p=0.04. The authors concluded that the results showed an increased risk for postoperative CSF leak when primary dural closure was not established. Creating a water-tight closure of the dura, regardless of dural substitutes and other dural overlays may be critical to decrease the risk of CSF leaks and postoperative outcomes. Due to the small sample size additional studies are needed to confirm the findings.

DuraMatrix -Onlay/ DuraMatrix-Onlay Plus, DuraMatrix Onlay and DuraMatrix Suturable

DuraMatrix (Collagen Matrix Inc, Oakland, NJ) is a suite of products derived from acellular bovine Achilles tendon. DuraMatrix Collagen Dura Substitute Membranes are indicated as dural substitutes for the repair of dura mater. DuraMatrix and has been cleared through the FDA's 510(k) process (K061487).

Mekonnen (2023) described a retrospective case series study involving 33 participants who underwent a duraplasty procedures using DuraMatrix-Onlay Plus collagen dura membrane. The majority of procedures were elective operations for the resection of a lesion (n=19, 58%). Average graft size was 17.69 ± 4.73 cm^2. At a mean follow-up of 3 months, no postoperative CSF leaks were reported. The rates of infection, dural substitute complication, and removal were 6%, 6%, and 3%, respectively. The clinical utility of this product warrants further investigation in more robust trials.

DuraMatrix Suturable (Collagen Matrix Inc, Oakland, NJ) is a product derived from bovine dermis collagen and is indicated for surgical dural repair and prevention of CSF leak. DuraMatrix Suturable is cleared through the FDA's 510(k) process (K061487).

DuraSorb

DuraSorb (Polydioxanone Surgical Scaffold) (Integra Lifesciences Corp., Princeton, NJ) is a fully-resorbable knitted mesh. It is indicated for use in reinforcement of soft tissue where weakness exists. DuraSorb is cleared through the FDAs 510(k) approval process (K181094).

ENDURagen

ENDURagen is a product composed of porcine acellular dermal matrix and iscleared through the FDA's 510(k) process (K013625).

McCord and others (2008) have published the only available study addressing the use of Enduragen. Their retrospective case series involved 69 participants who underwent 192 reconstructive or cosmetic eyelid procedures with Enduragen grafts. Eight procedures were for spacers in the upper lid, 104 were for spacers in the lower lid, and 17 were for lateral canthal reinforcement. There were 13 eyelid complications, for a complication rate of 10%. Nine cases required surgical revision, and there were four cases of infection, all of which were successfully treated with

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oral and topical antibiotics. The results of this study are insufficient to adequately evaluate the safety and efficacy of Enduragen. Further research is needed.

Barmettler (2018) published the results of a prospective, randomized clinical trial involving 39 participants (42 eyelids) undergoing lower eyelid retraction repair with spacer graft. Participants were assigned to undergo their procedure with autologous auricular cartilage (n=19 eyelids), SurgiMend (n=11 eyelids), or Enduragen (n=12 eyelids). The authors reported no significant differences between groups with regard to 6-month measures including MRD2, conjunctival injection, tearing, discomfort, itching, corneal abrasions, or repeat procedures.

Fortiva

Fortiva (RTI Biologics, Alachua, FL) is an implantable surgical mesh comprised of porcine dermis that has been processed, terminally sterilized and is stored hydrated and ready to use. The device is designed to perform as a scaffold that allows for neovascularization and permits replacement of the device with host tissue. Fortiva is intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes. Indications for use include the repair of hernias and /or body wall defects which require the use of reinforcing or bridging material to obtain the desired surgical outcome. The device is intended for single patient use only. Fortiva is cleared through the FDA's 510(k) process (K123356).

Maxwell (2019) published the results of a retrospective non-randomized controlled study investigating the use of Fortiva (n=72) compared to Strattice (n=98) and AlloDerm (n=59) in 229 participants undergoing abdominal wall reconstruction. The incidence of recurrence of abdominal wall defect was significantly higher in the AlloDerm group (20.3%) compared with the Fortiva (10.2%) and Strattice groups (6.9%) (p=0.040). The 1-, 3-, and 5-year survival rates for the repair with Fortiva were 1.4% and 6.9%, and 0%. For Strattice, the results were 5.1%, 9.2%, and 10.2%, and for AlloDerm, 6.8%, 18.5%, and 20.3%. Although participants in the AlloDerm group had the longest median hernia-free interval, 26.8 months (2-60 months), this was not found to be significantly different from Fortiva and Strattice (data not provided). The most common complication was surgical site infection (26.2%), followed by delayed healing (24.0%). Seroma formation was reported to have been significantly lower in the Fortiva group compared to the Strattice and AlloDerm groups (1.4% vs. 13.3% vs. 11.9%; p=0.021).

GalaFLEX

GalaFLEX mesh (TEPHA, Inc. Lexington, MA) is a sterile, knitted, synthetic, resorbable mesh product composed of poly-4-hydroxybutyrate. GalaFLEX mesh is indicated for use as a transitory scaffold for soft tissue support, and to repair, elevate, and reinforce deficiencies where weakness or voids exist, that require the addition of material to obtain the desired surgical outcome in plastic and reconstructive surgery, and general soft tissue reconstruction. GalaFLEX is cleared through the FDA's 510(k) process (K140533).

Adams (2018) published a case series report involving 62 participants undergoing mastopexy procedures. The authors reported that 89.7% of participants had successful ptosis correction and maintenance at 1 year. Both participant and surgeon satisfaction for breast shape, droop/sag of the breast, and maintenance of results at 1 year was reported as high. Adverse events deemed to be related to the device occurred in 5 participants (8.0%), including nerve pain, breast swelling, ptosis, and 2 instances of asymmetry. It is not clear how the safety and efficacy of this product compares to other products, including those considered the standard of care for breast

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procedures. Additional comparative trials are warranted.

Sigalove (2023) reported a retrospective case series of 263 individuals (499 breasts) who had immediate, two-stage expander-implant, prepectoral breast reconstruction that compared GalaFLEX plus AlloDerm combination (n=135/250 breasts) to AlloDerm only (n=128/249 breasts). In the GalaFLEX plus AlloDerm group the lower third of the expander was covered by the AlloDerm and the rest of the expander was covered by GalaFLEX Complications after reconstruction were compared between the groups. Mean BMI, preoperative chemotherapy use, skin reducing mastectomy, and bilateral reconstructions were higher in the AlloDerm only group, whereas nipple-sparing mastectomy and unilateral reconstructions were higher in the GalaFLEX plus AlloDerm group. Individuals in the AlloDerm-only group were followed up for an average of 41.9 months, whereas those in the GalaFLEX plus AlloDerm group were followed for an average of 15 months from the date of initial surgery ($p<0.0001$). Complications occurred in 19 breasts that received AlloDerm-only and 16 breasts that received GalaFLEX plus AlloDerm; overall complication rates were 7.6% and 6.4%, respectively. All complications occurred within the first year after initial surgery; 61% of individuals in the GalaFLEX plus AlloDerm group had at least 1 year of follow-up, and 17% had at least 2 years of follow-up. The rate of complication was 7.6% in the AlloDerm-only group and 6.4% in the GalaFLEX plus AlloDerm group. The rate of infection, major skin necrosis, seroma, capsular contracture, prosthesis exposure/extrusion, and prosthesis loss were less than or equal to 3.0% in the GalaFLEX plus AlloDerm group and did not differ significantly from those in the AlloDerm-only group. There were no significant differences in complications between the two groups with the exception of skin necrosis (5.2% for the AlloDerm-only group vs. 1.2% for the GalaFLEX plus AlloDerm group), which the authors noted was driven by a higher rate of intermediate skin necrosis. However, the rate of major skin necrosis did not differ significantly between the groups. The study is limited by its retrospective nature and the relatively short follow-up duration. The authors concluded that the GalaFLEX has a comparable safety profile, however additional long-term data and clinical experience are needed to comprehensively understand the safety profile of GalaFLEX bioabsorbable matrix for use in breast reconstruction.

Gentrix Surgical Matrix Thick and Gentrix Surgical Matrix Extend

The Gentrix devices (ACell, Inc., Columbia, MD) are products composed of porcine-derived extracellular matrix scaffolds, specifically known as urinary bladder matrix. Gentrix Surgical Matrix Thick and Gentrix Surgical Matrix Extend are intended for implantation to reinforce soft tissue where weakness exists in individuals requiring gastroenterological or plastic & reconstructive surgery. Reinforcement of soft tissue within gastroenterological and plastic & reconstructive surgery includes, but is not limited to, the following procedures: hernia and body wall repair, colon and rectal prolapse repair, tissue repair, and esophageal repair. The devices have been cleared through the FDA's 510(k) process (K170763).

Wang (2018) published a non-randomized controlled trial involving 65 participants who underwent paraesophageal hernia (PEH) repair with (n=32) or without (n=33) reinforcement with Gentrix. There was no difference reported between groups with regard to recurrence rates, size of recurrence, postoperative symptomatic or quality of life improvement. The authors noted that participants in the unreinforced group who suffered recurrence had more severe symptoms and a higher rate of dissatisfaction. Of the 3 participants with recurrences after Gentrix placement, reoperation demonstrated anterior failure where no reinforcement had occurred because of the posteriorly placed U-shaped graft. It is not clear how the safety and efficacy of this product compares to other products, including those considered the standard of care.

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Gore Bio-A

The Gore Bio-A Fistula Plug (W.L. Gore & Associates, Inc., Elkton, MD) is a surgical mesh comprised of porous synthetic copolymer fiber material that is bioabsorbable and has been demonstrated to be both biocompatible and non-antigenic. The device is intended for use in the reinforcement of soft tissue for the repair of anorectal fistulas. Gore Bio-A is cleared through the FDA's 510(k) process (K083266).

Ommer and others published the results of a case series study involving 50 participants with trans-sphincteric (n=28) or supra-sphincteric (n=12) anal fistula who were treated with Gore Bio-A (2012). Postoperatively, 1 participant developed an abscess which had to be managed surgically. In 2 participants, the plug had fallen out within 2 weeks after surgery. Six months after surgery, the fistula had been healed in 20 participants (50.0%). Three additional fistulas healed after an additional 7 to 12 months. The authors reported that the overall healing rate was 57.5% (23/40). However, they noted that healing rates differ significantly between the surgeons (from 0 to 75%), and also varied depending on the number of previous interventions. In individuals having had only drainage of the abscess, success occurred in 63.6% (14/22) whereas, in those having had one or more flap fistula reconstructions, the healing rate decreased slightly to 50% (9/18). Further study is warranted to better understand the impact of surgeon experience as well as optimal selection criteria for individuals requiring treatment for anal fistulas. Heydari (2013) described the results of a retrospective case series study involving 48 participants with 49 anal fistulas treated with the Gore Bio-A. The overall healing rate was reported to be 69.3% (34/49 fistulas, 33/48 participants). Eight participants (24.2%) had complete healing by 3 months after surgery, 21 participants (63.6%) had healed by 6 months, and 4 participants (12.1%) had healed by 12 months. At 3 months, there were no reports of perineal pain or fecal incontinence. The authors reported no incidents of dislodged devices, anal stenosis, bleeding, or local infection.

In 2018 Jordan and others published the results of a retrospective comparative study involving 87 participants undergoing breast reconstruction with mesh underlay reinforcement at 123 sites with either polypropylene mesh (n=58) or Gore Bio-A (n=65). The overall incidence of bulge or hernia was 11.4%. The Gore Bio-A group experienced significantly more bulges/hernias than the polypropylene mesh group (20% vs. 1.7%). They concluded that the use of Gore Bio-A was associated with a 13.3-fold risk of bulge/hernia (p=0.016) and was not appropriate for anterior rectus fascia reinforcement following abdominal tissue transfer.

In 2017, the American Society of Colon and Rectal surgeons published a new Practice guideline for the management of anal fissures (Stewart, 2017). Their recommendations do not mention the use of grafts or plugs of any kind.

Gore ACUSEAL Vascular Graft

Gore Acuseal Vascular Graft Patch (W.L. Gore & Associates, Inc., Elkton, MD) is an expanded polytetrafluoroethylene (ePTFE) separated by an elastomeric layer and may be available both with and without covalently bound bioactive heparin. The GORE ACUSEAL Vascular Graft is intended for use as a vascular prosthesis in individuals requiring vascular access. It has been cleared through the FDA's 510(k) process (K130215).

Stone (2014) published the results of a prospective randomized study comparing clinical outcomes of Acuseal compared to bovine pericardium patching (Vascu-Guard) when used for primary closure for carotid

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endarterectomy. This study involved 200 participants assigned in a 1:1 fashion and the mean follow-up period was 15 months. They reported that mean hemostasis time was 4.90 min for Acuseal vs. 3.09 min for Vascu-Guard (p=0.027). The mean operative times were similar for both groups (2.09 hr vs. 2.16 hr, p=0.669). The incidence of reexploration for neck hematoma was higher in the Vascu-Guard group; 6.12% vs. 1.03% (p=0.1183). The incidence of perioperative ipsilateral neurologic events was 3.09% for Acuseal patching compared to 1.02% for Vascu-Guard patching (p=0.368). The respective freedom from ≥ 70% carotid restenosis at 1, 2, and 3 years were 100%, 100%, and 100% for ACUSEAL patching compared to 100%, 98%, and 98% for Vascu-Guard patching (p=0.2478).

AbuRahma (2023) reported on the 10-year results of the study previously published by Stone et al. (2016). Mean follow-up time was 81 months (range 0-149 months). No significant differences were reported between groups for rates of long-term death, 47% in the Acuseal group compared to 48% in the Vascu-Guard group p=0.9402). Similarly, the incidence of late strokes was reported to be 5% in both groups (p=1.0). One patch complication was noted in the Acuseal group (infection) compared to the Vascu-Guard group (aneurysmal dilatation and rupture, no p-values provided). No significant differences in the rate of reintervention was reported (5% in the Acuseal group compared to 4% in the Vascu-Guard group, no p-values provided). The rate of ≥50% restenosis was 9% for the Acuseal group compared to 22% for Vascu-Guard group (p=0.0186). The rates of ≥80% restenosis, freedom from stroke, freedom from stroke/death, freedom from ≥80% restenosis, and overall survival rates were all not significantly different between groups for any time point (p=0.564, p=0.1112, p=0.8591, p=0.9407, p=0.9123, respectively). The authors concluded that both product are durable and have similar clinical outcomes at 10 years, except that ACUSEAL patching has significantly better rates of freedom from ≥ 50% restenosis.

Grafix CORE

Grafix CORE is a grafting product derived from allogeneic chorion membrane. It is treated as human tissue for transplantation under the FDA's HCT/P process.

Frykberg (2016) reported the results of a prospective case series study involving participants with complex DFUs ≤ 15 cm in their longest dimension and extending through the dermis with exposed muscle, tendon, fascia, bone, or joint capsule. All were treated with weekly applications of Grafix CORE. The intent-to-treat (ITT) population included 31 participants and the per-protocol population included 27 participants. The ITT participant population had significant co-morbidities, with 80% having hypertension, 60% current or former smokers, 55% having heart disease, and 45% having a previous partial foot amputation. Prior advanced treatment (for example, negative pressure wound therapy) for the index wound had occurred in 67.7% of participants. At 16 weeks, 96.3% of the per-protocol group had 100% granulation of the index wound and complete closure occurred in 59.3%. The mean area reduction of the index wound at day 28 was 54.3% and 72.8% at 8 weeks. At the end of the 16-week study period the mean wound area reduction was 92.3%. No Grafix-related adverse events were reported. This study demonstrated the use of Grafix CORE in the healing of complex DFUs. However, the small study population and lack of controls hampers the generalizability of these results.

Raspovic (2018) reported a retrospective case series analysis of 360 participants with 441 DFUs treated with Grafix PRIME or Grafix CORE using data from Net Health's Wound Expert electronic health records database. The mean size of the index wound was 5.1 cm^2 with 3.9 mm depth. Mean wound duration prior to study treatment was 102 days. The mean duration of treatment with a Grafix product was 89.3 days (median 56.0). Complete wound closure at the end of treatment occurred in 59.4% of participants. Median time to closure was 42.0 days with a median of 4

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graft applications. The proportion of closure decreased as wound size increased, with 72.3% of wounds between 0.25 cm^2 to 2 cm^2 having complete healing at a median of 21 days and 4 applications. For wounds larger than 25 cm^2, only 27.8% achieved complete healing at a median of 105 days and 11 applications. The authors did not provide any data regarding the percentage of participants receiving treatment with Grafix PRIME compared to those receiving Grafix CORE.

Helicoll

Helicoll (Encoll Corp., Freemont, CA) is a bioengineered reconstituted collagen sheet that maintains a physiologically moist microenvironment at the wound surface. Helicoll is intended for the topical wound management that includes: partial and full-thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds (abrasions, lacerations, second-degree bums, skin tears), and surgical wounds (donor sites/grafts, post-Mohs' surgery, post-laser surgery, podiatric, wound dehiscence. The device is intended for one time use only. It is cleared under the FDA 510(k) process (K040314).

A randomized controlled clinical trial by Narayan (2024) enrolled 28 individuals with DFUs and compared Helicoll to an unspecified dehydrated human amnion and chorion membrane product over 4 weeks. The study showed that 85.71% (12/14) of participants in the Helicoll group achieved at least a 50% reduction in DFU size, compared to 50% (7/14) in the dehydrated membrane group (p=0.245). Complete closure was observed in 10 and 7 participants, respectively. The Helicoll group demonstrated a mean DFU size reduction of 86.48%, while the dehydrated membrane group recorded 77.70%. The authors noted that their statistical analysis indicated a significant difference in mean wound reduction rates (93.62 ± 0.12% vs. 77.71 ± 0.28%, p=0.05), suggesting enhanced wound-healing capabilities for Helicoll in managing DFU.

Hyalomatrix

HYALOMATRIX is a synthetic wound covering product composed of a benzyl ester of hyaluronic acid. HYALOMATRIX is indicated for the management of wounds including partial and full-thickness wounds, second-degree burns, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds, trauma wounds, and draining wounds. The device is intended for one-time use. HYLAOMATRIX is approved through the FDA's 510(k) process (K073251).

The currently available evidence addressing the use of HYALOMATRIX is limited mostly to uncontrolled, unblinded case series studies. Only one RCT has been published to date involving 16 participants with VSUs, 9 of which were treated with HYLAOMATRIX and 7 treated with standard wound care (Alvarez, 2017). The authors reported that the incidence of wound healing at 12 weeks was 66.6% for the HYALOMATRIX group compared to 14.2% for controls (p=0.066). At 16 weeks, the incidence of wound healing was 87.5% of participants in the HYALOMATRIX group compared to 42.8% in the control group (p=0.059). The mean time to healing in the Hyalomatrix group was 41 days compared with 104 days in the control (p=0.029). The largest studies available involve 300, 262, 79, and 57 participants (Gravante, 2007; Caravaggi, 2003 and 2011; Gravante 2010, respectively). The Carravaggi study addresses chronic wounds while the Gravante studies address burns. The rest of the studies published involve significantly fewer than 30 participants and encompass a variety of indications including various surgically created wounds (Faga, 2013; Landi, 2014; Onesti, 2014), traumatic wounds (Kozusko, 2023; Onesti, 2014; Vaienti, 2013), and chronic ulcers (Motolese, 2013).

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Integra Bilayer Matrix and Integra Flowable Wound Matrix

Integra Bilayer Matrix Wound Dressing (Integra Lifesciences Corp., Plainsboro, N.J.) is comprised of granulated cross-linked bovine tendon collagen, glycosaminoglycan, and a semipermeable silicone layer. The product is indicated for the management of wounds including partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, skin tears) and draining wounds. The device is intended for one-time use. It was cleared through the FDAs 510(k) process (K021792).

Integra Flowable Wound Matrix (Integra Lifesciences Corp., Plainsboro, N.J.) was also cleared through the FDAs 510(k) process (K072113). It is comprised of granulated cross-linked bovine tendon collagen and glycosaminoglycan. The product is indicated for the management of wounds including partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, skin tears) and draining wounds. The device is intended for one-time use.

In 2017, Campitiello published an RCT comparing Integra Flowable Wound Matrix compared to standard care for the treatment of 46 participants with DFUs with irregular geometries. There were 23 participants in each group who were evaluated once a week for 6 weeks. The authors reported that the overall complete healing rate was 69.56%, with the rate in the Integra group being 86.95% compared to 52.17% in the control group (odds ratio [OR], 1.67, p=0.001). Mean time to healing was 29.73 days in the Integra group compared to 42.78 in the control group (p<0.000). The amputation and rehospitalization rates in the Integra group were 4.34% compared to 30.43% in controls (relative risk [RR], 0.16, p=0.028). The authors concluded that Integra Flowable Wound Matrix was significantly superior to the wet dressing, but that additional research will shed more light on the promising advantages of this material in healing diabetic foot ulcers.

KeraMatrix

KeraMatrix (Keraplast Technologies, LLC., San Antonio, TX) is comprised of freeze-dried acellular animal-derived keratin and has been approved through the FDA's 510(k) process (K080949).

At this time, the most rigorous evidence is a nonrandomized controlled study involving 40 participants with superficial or partial thickness burn injuries treated with Keramatrix, compared to 40 historical controls who received standard of care treatment (Loan, 2016). The results indicated a significantly faster mean healing time in the Keramatrix group compared to controls (8.7 days vs. 14.4 days, p<0.05), hospital inpatient days (0 days vs. 2.6 days, p<0.05), and number of outpatient appointments following initial therapy (1.2 vs. 3.3, p<0.05). No differences in complications were reported.

MatrACELL

MatrACELL is a decellularized allograft product composed of human cardiovascular tissue treated as human tissue for transplantation under the FDA's HCT/P process.

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Hopkins (2014) published a nonrandomized controlled study involving 108 consecutive participants undergoing cardiovascular reconstructive procedures using MatrACELL pulmonary artery patches during pulmonary arterioplasty. A second retrospective cohort of 100 participants who received arterioplasty patches using classical cryopreserved pulmonary artery allografts (n=59 participants) or synthetic materials (n=41 participants) was used for comparison. The reported results included that 106 participants with 118 decellularized patches had no device-related serious adverse events, no device failures, and no evidence of calcifications on chest roentgenograms. In contrast, the control participants experienced an overall 14.0% patch failure rate requiring device-related reoperations ($p<0.0001$) at mean duration of 194 ± 104 days (range, 25 to 477 days). The authors concluded that the intermediate-term data obtained in this study suggest favorable performance by decellularized pulmonary artery patches, with no material failures or reoperations provoked by device failure.

MatriDerm

MatriDerm is a decellularized dermis allograft product treated as human tissue for transplantation under the FDA's HCT/P process.

Riml (2011) reported a study of 30 participants undergoing nasal tip skin grafts non-randomly assigned to receive either conventional FTSG, retroauricular perichondrodermal composite grafts, or skin transplantation supplemented with MatriDerm. Ten participants were assigned to each group. This retrospective study was conducted in a randomized and blinded manner by assigned reviewers using the Manchester scale. The authors report that 2 (20%) of the MatriDerm participants developed fistulae and concluded that MatriDerm was not suitable for nasal tip reconstruction.

Another study by Haslik evaluated the use of MatriDerm for the management of full-thickness skin defects (2010). This case series study involved 17 participants with upper extremity skin wounds, all of whom received MatriDerm in conjunction with unmeshed skin grafts. The reported take rate was 96%. A 12-month follow-up Vancouver scale score of 1.7 and DASH (disability of arm-shoulder-hand) score showed excellent hand function in participants with burn injury and participants with a defect due to the harvest of a radial forearm flap achieved satisfying hand function.

Wallner (2023) published a retrospective study that compared the use of single autologous split-thickness skin graft (STSG) alone or in combination with MatriDerm ADM in 147 cases of severe traumatic soft tissue defects of the leg with exposed structures, such as tendons, ligaments, vessels, bone of the lower extremities. Severe soft tissue defects consisted of 18 open fractures with extensive decollement, 43 thermic and chemical burns, 78 severe soft tissue lesions, and 8 ulcers. Overall, soft tissue defects were more severe in the MatriDerm plus STSG group. The healing rate, defined as the number of individuals with take rate ≥ 75%, was 88/147 (60%) and no significant differences between the groups was reported ($p=0.15$). Despite variable wound complexity between the groups there were no differences in scar tissue quality 12 months postoperatively. The overall complication rate was approximately 25%. In 15% of the cases, a surgical revision was required. The number of cases with at least one necessary surgical revision was 4 in the STSG-only group compared to 18 in the MatriDerm plus STSG group ($p=0.02$). The number of individuals with documented adverse events (33%) or necessary revision surgery (21%) was higher in the STSG plus MatriDerm group. The complications reported after more than 100 days included scar instability, fistula formation, and swelling. Additionally, the use of negative pressure wound therapy may have impacted the STSG take rate. The authors concluded that surgical treatment with STSG and additional MatriDerm application is a satisfactory alternative for dermis replacement in individuals with severe skin defects, independent

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of age. Due to the higher rate of adverse events, complications, and surgical revision, further studies with larger, well-designed trials are needed to fully evaluate the safety and efficacy of MatriDerm..

In a retrospective single-center original article, Do (2024) evaluated 12 individuals who underwent maxillectomy for oral cancer treated with a combination of MatriDerm and Neoveil. Over a follow-up ranging from 2 to 20 months, 41.7% of participants experienced fistula formation, but no surgical revisions were required. The incidence of fistulas depended on tumor stage, bone invasion, defect dimensions, and sinus mucosa preservation ($p<0.05$), rather than product-specific performance. None of the participants developed mouth-opening limitations, indicating potential benefits of the combined technique. However, since this study combined Matriderm and Neoveil in all participants, the relative benefits of each product alone cannot be determined and further research is needed.

MediHoney

The use of honey has been proposed for the treatment of various skin conditions including burns, chronic ulcers, and superficial abrasions. It is hypothesized that honey, with its antibacterial properties, can significantly improve skin healing when applied topically to skin wounds. Several randomized controlled trials have been published involving MediHoney (Derma Sciences, Princeton, N.J.). Medihoney is cleared through the FDA's 510(k) process (K072956).

Jull (2008) published the largest of these trials, which included 368 participants randomized to receive treatment with either calcium alginate dressing impregnated with manuka honey or standard care with whatever dressings were appropriate for the individual at that time. After following the participants for a total of 12 weeks of follow-up, the authors concluded that there was no significant difference in outcomes between the two groups. It was noted that the honey-treated group experienced significantly greater numbers of adverse events ($p=0.013$). Contradicting these findings is a study by Gethin and Cowman (2008). In this study, 108 participants with venous ulcers were randomized to receive treatment with either honey dressing or standard hydrogel therapy. The findings were that the honey-treated group had significantly better results in terms of median reduction in wound size at 12 weeks (44% vs. 33%, $p=0.037$), but no significant differences between groups in other primary endpoints were reported.

The other most studied condition addressed in the literature is the treatment of burns. The largest study currently available addressing burns involved 150 participants randomized to receive treatment with either silver sulphadiazine (SSD) or honey (Malik, 2010). Each participant functioned as his or her own control, with one burn site randomly treated with SSD and the other with honey. The authors report that the honey-treated sites had significantly faster re-epithelialization and healing of superficial and partial thickness burns than the SSD sites (13.47 days vs. 15.62 days, $p<0.0001$). Additionally, the honey-treated sites achieved complete healing significantly faster than SSD sites (21 days vs. 24 days, $p<0.0001$).

Lund compared the use of honey-coated dressing for breast malignant wounds. In this study, 67 participants, 79% of whom had breast cancer, were randomized to receive treatment with either honey-coated dressing (n=34) or silver dressing (n=33). The authors report no significant differences between groups, and they concluded that the possible antibacterial effect of either treatment "could not be confirmed in these malignant wounds."

MegaDerm

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MegaDerm Plus (L & C Bio, Seoul, Korea) is a suite of products (MegaDerm Plus, MegaDerm HD, MegaFill, MegaSheet) made from acellularized human skin-derived acellular dermal matrix (ADM) allograft, and is regulated through the FDA's HCT/P process as human tissue for transplantation.

In 2012 Kim reported on a prospective non-randomized study investigating the use of MegaDerm in parotidectomy procedures involving 109 participants who underwent treatment with Megaderm (n=58) or no implant (n=51). Decision on what group the participants were allotted was made by the participant in consultation with the surgeon. The study initially enrolled 134 participants but 25 were lost to follow-up. The authors reported a significantly higher rate of seroma at postoperative week 1 in the Megaderm group compared to the control group (14 vs. 6, respectively, p=0.22). However, no significant differences between groups were reported with regard to other complications, including infection (p=1.0), Hematoma (p=0.182), skin necrosis (p=1.0), and pain (p=0.28). Additionally, no difference between groups were reported with regard to patient-reported Frey's syndrome quality scores at 3, 6, and 12 months. However, the incidence of Frey's syndrome was significantly higher in the MegaDerm group at 3, 6 but not 12 months (p=0.32, 0.037 and 0.28, respectively). The authors stated that the use of MegaDerm for parotidectomy procedures, however, the higher rate of seroma is of concern and should be further evaluated in studies with less potential for selection bias.

In 2017, Kim retrospectively assessed 73 individuals to determine whether Megaderm (n=29) could replace absorbable mesh (n=22) or porous polyethylene (n=22) in orbital wall reconstruction. Enophthalmos, range of eyeball movement, diplopia, and infraorbital nerve numbness were evaluated at 1 and 3 weeks, and 3 and 6 months. At 6 months, complete resolution of all of these measures was reported in all groups (p=1.0). The most common complication was transient and self-limited diplopia, which developed in the early postoperative stage, one in the mesh group and 2 in the polyethylene group. No MegaDerm group participants developed diplopia. Infraorbital numbness was observed in 1 mesh group participant and 1 polyethylene group participant. Transient and self-limited lagophthalmos was reported in 1 mesh group participant. No p-value was provided for these intergroup comparisons. The authors concluded that MegaDerm, based on the results of this study, would be an excellent alternative material for orbital wall reconstruction. However, additional research is needed to verify these findings in a more robust trial.

Park (2023) retrospectively compared freeze-dried Megaderm to pre-hydrated Megaderm in 78 individuals undergoing immediate implant-based breast reconstruction with latissimus dorsi muscle coverage. The freeze-dried form was used in 26 individuals, while 52 individuals received the pre-hydrated product. The overall complication rate did not differ significantly, 30.8% in the freeze-dried group compared to 55.8% in the pre-hydrated group (no p-value provided). Seroma was more frequent in the pre-hydrated ADM group (n=20 vs. 4) but the difference between the two groups was not statistically significant (p=0.120). The pre-hydrated version showed a higher mean shape score of 3.46 plus or minus 0.5 compared to 3.08 plus or minus 0.7 in the freeze-dried cohort (p=0.019). The authors concluded that while complication rates were similar between pre-hydrated ADM and freeze-dried ADM, aesthetic outcome was better in pre-hydrated ADM in terms of symmetry. Further investigation into the use of MegaDerm and its variants are needed to better understand the clinical utility of this product.

In a single-blind, randomized, controlled trial published in 2024, Han evaluated 56 individuals undergoing immediate prepectoral direct-to-implant breast reconstruction using Megaderm with and without a basement membrane. Specifically, 30 participants received Megaderm HD (with basement membrane) and 26 participants received Megaderm Flex HD (without basement membrane). The total drainage volume was 893 milliliters plus or minus 399 in the Megaderm HD group compared to 859 milliliters plus or minus 341 in the Megaderm Flex HD

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group (p=0.74). Drains were removed at approximately 17 to 18 days. No significant differences between groups were observed in terms of overall complication rates between the 2 groups (26.7 vs. 23.1, respectively, p=0.76), the rate of seromas (3 vs. 0, respectively, p=0.09),infection (1 vs. 0, respectively, p=0.35), wound dehiscence (2 vs. 3, respectively, p=0.52), mastectomy flap necrosis (0 vs. 1, respectively, p=0.28), or capsular contracture (3 vs. 2, respectively, p=0.76). The authors concluded that Megaderm Flex HD in implant-based breast reconstruction was safe.

Menaflex (formerly "Collagen meniscus implant" or CMI)

Collagen meniscus implants (e.g., Menaflex) have been proposed as a treatment method for individuals with a damaged knee meniscus. Menaflex is a human-derived acellular collagen product treated as human tissue for transplantation under the FDA's HCT/P process.

Rodkey (2008) published a study with 311 participants with irreparable injury of the medial meniscus or a previous partial medial meniscectomy. The study population was divided into two groups, those with prior meniscal surgery (chronic group) and those with no prior surgery (acute group). These populations were further randomized to receive either treatment with a collagen meniscus implant or a partial meniscectomy only. The mean duration of follow-up was 59 months (range, 16 to 92 months). Repeat arthroscopies done in the experimental group at 1 year showed significantly (p=0.001) increased meniscal tissue compared with that seen after the original index surgery. In the chronic group, participants who had received the collagen implant regained a significantly higher degree of pre-surgery activity than did the controls (p=0.02). This group also underwent significantly fewer non-protocol reoperations (p=0.04). The authors reported no significant differences between the two treatment groups in the acute arm of the study.

Zaffahnini conducted a long-term trial of the performance of the Menaflex implant in 33 participants. This nonrandomized controlled trial allowed participants to choose treatment with either Menaflex (n=17) or partial medial meniscectomy (n=16). Participants were evaluated at baseline, 5 years and then 10 years after surgery. At 10 years, the authors report that the Menaflex group showed significant improvement compared to meniscectomy with regard to visual analog scale for pain (p=0.004), International Knee Documentation Committee knee form (p=0.0001), Teger index (p=0.026), SF-36 Physical Health Index (p=0.026), and SF-36 Mental Health Index (p=0.004). Radiographic evaluation showed significantly less medial joint space narrowing in the Menaflex group than in controls (p=0.0003). There were no significant differences reported between groups regarding Lysholm score (p=0.062) and Yulish score (p=0.122). Genovese score remained constant between 5 and 10 years after surgery (p=0.5).

Another case series study of 22 participants followed for 10 years was reported by Monllau (2011). The results of this study demonstrated that several measures improved, including the visual analog pain scale and radiographic joint line narrowing. The Lysholm score was significantly improved, from 59.9 at baseline, 89.6 at 1 year ($p<0.001$), and 87.5 at 10 years ($p<0.001$). Failure rate was only reported to be 8% in the 25 participants initially implanted.

Van Der Straeten published the results of a cohort study of 313 participants who received treatment with the collagen meniscal implant and were followed for a mean follow-up of 6.8 years (2016). A total of 56.5% of the implants were still intact and in place; 27.4% had been removed. This included 63 implants converted to a knee arthroplasty (19.2%). The overall cumulative allograft survivorship was 15.1% at 24.0 years. Simultaneous

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osteotomy significantly deteriorated survival (0% at 24.0 years) (p=0.010). The authors stated that 61% of participants underwent at least one additional surgery (range 1-11) for clinical symptoms after implantation. They concluded that the collagen meniscal implant did not delay or prevent tibiofemoral OA progression.

Another large cohort study was reported by Waterman (2016). This study involved 230 active-duty military personnel who underwent treatment with the collagen meniscal implant. A total of 51 complications occurred in 46 (21.1%) participants, including a secondary tear or extrusion (9%). The authors reported that 10 participants (4.4%) required secondary meniscal debridement at a mean of 2.14 years. Revision was done in 1 participant (0.4%) and 20 participants (0.9%) subsequently underwent total knee arthroplasty. After implantation, 50 participants (22%) underwent knee-related military discharge at a mean of 2.49 years postoperatively. They concluded that while there were low reoperation and revision rates, their investigation indicated that 22% of participants who received implants were unable to return to military duty due to persistent knee limitations at short-term follow-up.

Menaflex was originally cleared by the FDA in the 510(k) process. Subsequent to further review by the FDA, this clearance was revoked. The manufacturer, ReGen Biologics, Inc. went bankrupt shortly thereafter. The Menaflex device is currently not marketed in the U.S.

Miro3D

Miro3D Wound Matrix (Reprise Medical, Plymouth MN) is a sterile, single use, non-crosslinked porcine acellular wound dressing. The Miro3D porous scaffold provides a protective environment for wound healing. The device is packaged dry, terminally sterilized in its packaging by e-beam irradiation, and is rehydrated with sterile saline or lactated Ringer's solution prior to use. Miro3D Wound Matrix is provided in four sizes that may be cut to fit a wound size prior to application. Miro3D is indicated for partial and full thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, tunneled, undermined wounds, trauma wounds (abrasions, lacerations, partial-thickness burns, and skin tears), draining wounds, and surgical wounds (donor sites/grafts, post-Mohs' surgery, post-laser surgery, podiatric, wound dehiscence). Miro3D is cleared through the FDA's 510(k) process (K223257).

In a retrospective case series by Abdo (2024), 11 individuals with type 2 diabetes and 13 deep or tunneling foot ulcers present for at least 4 weeks underwent surgical debridement and application of Miro3D. One individual also underwent are with the Miro3D Fibers Wound Matrix product. Over the 4-week study period, 62% (8/13) of ulcers achieved at least 50% area reduction by 4 weeks, and 54% (7/13) closed fully by 12 weeks, with all ulcers ultimately healing in an average of 13.1 weeks (range 2.0–22.3 weeks). Participants with larger initial volumes and poor offloading adherence tended to take longer to heal. However, no new infections, readmissions, or adverse events linked to Miro3D were reported. The concluded that the results suggest that Miro3D Wound Matrix effectively creates a protective environment for managing deep or tunneling DFUs, with early improvements in depth and volume. However, the study's retrospective design and relatively small sample size and other methodological issues limit broader generalizability, and further research is needed.

MiroTract

MiroTract (Reprise Medical, Plymouth MN) is a porcine-derived collagen wound matrix compressed on a guidewire and expands when hydrated to fit the wound bed. It is a porous three dimensional structure indicated for partial and full thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, tunneled,

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undermined wounds, trauma wounds (abrasions, lacerations, partial-thickness burns, and skin tears), draining wounds, and surgical wounds (donor sites/grafts, post-Mohs' surgery, post-laser surgery, podiatric, wound dehiscence). MiroTract is cleared through the FDA's 510(k) process (K231614).

Myriad Matrix and Myriad Morcells

Myriad Matrix and Myriad Morcells are comprised of processed ovine forestomach matrix. Myriad Morcells are intended to cover, protect, and provide a moist wound environment. The products are indicated for the management of partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, partial-thickness burns, and skin tears), and draining wounds. The products are cleared through the FDA's 510(k) process (K200502).

Two studies published in 2023 are the first to address the clinical utility of Myriad. Cormican (2023) reported the results of a retrospective pilot case series involving 10 participants with 13 contaminated lower-extremity defects undergoing surgical reconstruction with Myriad Matrix (n=3), Myriad Morcells (n=4), or both (n=6). All participants had at least 1 significant comorbidity with the potential to complicate their healing trajectory. Mean defect age was 3.5 ± 5.6 weeks and mean area was 217.3 ± 77.9 cm^2. Most defects had exposed structures (85%), and all defects were Centers for Disease Control and Prevention grade 2 or higher. Mean time to 100% granulation tissue formation was 23.4 ± 9.2 days, with a median product application of 1.0. Staged reconstruction was used in 7 of 13 defects, with the remainder (6 of 13) left to heal via secondary intention using standard wound care protocols. Mean follow-up was 7.4 ± 2.4 weeks, with 4 wounds (30%) lost to follow up ≤ 5 weeks. No major postoperative infections or adverse events were reported. The small sample size, and high loss to follow-up do not allow reasonable, generalizable conclusions regarding the clinical utility of these products

Bosque (2023) described the results of a similar retrospective case series study involving 50 participants with complex lower-extremity defects undergoing surgical reconstruction with Myriad Matrix (n=41), Myriad Morcells (n=3), or both (n=6). The participants had heterogenous etiologies, including diabetic foot ulcers (DFUs) (48%), half of which were complicated by a necrotizing soft-tissue infection (50%). Additionally, in the total population, 34% of participants had exposed bone, 10% had exposed tendon, 18% had both exposed tendon and bone, and 4% had exposed capsule. Ten participants (20%) were lost to follow-up before complete closure of the defect, but after 100% granulation tissue had formed. Where Myriad products were used for dermal regeneration (n=47), the median time to 100% granulation tissue was 17 days (mean, 26 ± 22.2 days; range, 7–120 days). A total of 38 participants (76%) were closed by secondary intention, with an overall median time to close of 14 weeks (mean, 14.0 ± 5.9 weeks; range, 1–27 weeks). The overall time to closure from the initial surgical procedure to closure across defects (n=40) was 13 weeks (mean, 13.7 ± 6.9 days; range, 2–29 weeks). This study involving these two Myriad products is promising, but the results are limited by multiple factors, including significant loss to follow-up, heterogeneity of wound etiologies, and use of multiple versions of the product used.

NEOVEIL

NEOVEIL Tube/Sheet (Gunze Limited, Kyoto, Japan) is a synthetic surgical mesh made from bioabsorbable polyglycolic acid (PGA), designed for use in surgical procedures that require reinforcement of soft tissue transection or resection with staples or sutures. NEOVEIL is indicated for use in surgical procedures in which soft tissue transection or resection with suture or staple line reinforcement is needed. The product can be used for

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reinforcement of suture or staple lines during lung resection, liver resection, bronchial, bariatric, colon, colorectal, esophagus, gastric, mesentery, pancreas, and small bowel procedures. NEOVEIL has received clearance under the FDA 510(k) process (K130997).

NeuraGen Nerve Guide

NeuraGen 3D Nerve Guide Matrix (Integra LifeSciences Corporation, Plainsboro, N.J.) is a resorbable implant for the repair of peripheral nerve discontinuities. NeuraGen 3D is composed of bovine Type I collagen conduit and a porous inner matrix comprised of collagen and glycosaminoglycan (chondroitin-6-sulfate). NeuraGen 3D is supplied sterile, non-pyrogenic, for single use. NeuraGen 3D provides a protective environment for peripheral nerve repair after injury, and is designed to isolate and protect the nerve and to create a conduit for axonal growth across a nerve gap. The NeuraGen 3D is indicated for the repair of peripheral nerve discontinuities where gap closure can be achieved by flexion of the extremity. The device is cleared through the FDA's 510(k) process (K163457).

In an unblinded RCT of Neuragen 44 participants with ulnar or median nerve lacerations were assigned to treatment with Neuragen (n=23) compared to direct fascicular repair or nerve grafting (n=21) (Boeckstyns, 2013). The authors reported that data for only 36 participants (81%) were available at the 24-month follow-up visit. However, they do not provide information regarding which groups the dropouts were from. At 24 months no significant differences between groups were reported with regard to amplitudes, latencies and conduction velocities. With regard to comparison to the contralateral hand, both groups remained significantly deficient on all electrophysiological measures. No surgical complications were reported. These results may indicate some benefit from the use of Neuragen, but the generalizability is hampered by missing information regarding participants at 24 months, as well as methodological flaws such small study population and lack of blinding.

In addition to this study, several unblinded non-randomized controlled trials and multiple case series studies addressing the use of Neuragen have been published, with most involving small numbers of participants (Ashley, 2006; Bushnell; Distinct, 2013; Erakat 2013; Farole, 2008; Haug 2013; Huber 2017; Karup, 2017; Lohmeyer, 2014; Rbia, 2019; Schmauss 2014; Taras, 2011; Wangensteen, 2010; Wilson, 2016). These studies do not adequately control bias and the clinical utility and generalizability of their conclusions is limited.

Subsequently, Ilyas (2024) reported a multicenter US based RCT that included 220 participants with digital nerve injuries, treated either with type I bovine collagen conduit (CONDUIT) or a PNA. The CONDUIT group used the NeuraGen Nerve Guide, whereas the PNA group used the Avance Nerve Graft. Inclusion criteria were individuals 18- to 69-years with 5 to 25 mm digital nerve gaps within 24 weeks of injury. Participants were randomized (1:1) to PNA or CONDUIT repairs. Cold Intolerance Symptom Severity (CISS) scores and sensory function testers were assessed at first visit (FPV), 1-, 3-, 6-, 9-, and 12-months post-surgery, both participants and assessors blinded to treatment. One hundred eighty-three participants completed the last evaluable visit (LEV) of 6 months or more of follow-up; of these, 91 received PNA repair and 92 had CONDUIT repair. No significant differences were observed in demographics, gap length, time to repair, or injury mechanism between the groups. The average gap lengths were 13.6 mm for the PNA group and 13.0 mm for the CONDUIT group. The average time to repair was 28.2 and 23.4 days for repairs, respectively. Both groups reported a reduction in the CISS over time, indicative of improved cold intolerance symptoms. The mean CISS score for the entire cohort decreased from 31.15 ± 29.25 at FPV to 23.42 ± 22.16 at the LEV. The reduction in CISS score was numerically greater but not statistically different in the PNA group (10.39 points) compared with the CONDUIT group (5.23 points). A sub-analysis

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showed more participants improved from severe/extremely severe cold intolerance to mild cold intolerance for PNA compared with CONDUIT at 1 month and LEV ($p< 0.05$). The CISS scores also correlated with sensory function testing. The authors concluded that PNA had improved cold tolerance outcomes for participants with more severe cold intolerance at FPV relative to nerves repaired with CONDUIT. The study was limited by a loss to follow-up at later timepoints in the study. At the 1-month timepoint, the study had a total of 178 participants, but by 12 months, only 149 were available for evaluation. Target follow-up for the study was 12 months, however, participants were assessed at or greater than 6 months, which included up to 15 months out from repair. The study did not include a sub-analysis of participants who concomitantly underwent vascular repair. This was due to a low overall number of participants with vascular injury requiring repair, which is likely a result of the exclusion criteria of the study as well as study design limitations. This limits the generalizability of this study to patients with nerve injuries who do not require vascular repair.

Neuro-Patch

Neuro-Patch device (B. Braun Medical Inc., Bethlehem, PA) is a synthetic fabric composed of fine-fibered microporous polyester urethane fleece. Neuro-Patch is indicted as a dura mater substitute in neurological procedures for soft tissue reconstruction of damaged, impaired or missing tissue. It is cleared through the FDA's 510(k) process (K960470).

A non-randomized comparative study was published by Wales (2024), involving 11 participants, (6 who prospectively received treatment with Neuro-Patch and 5 retrospective participants treated with autologous grafts). In the Neuro-Patch group, the authors reported no cerebrospinal fluid leaks, need for lumbar drains, or hearing loss by the 6 month follow-up. Discharge occurred within 48 hours in all participants in this group, with no readmissions. By contrast, the control group had a higher rate of complications, including two instances of CSF leak with lumbar drains placement. They reported an average inpatient stay or 91.2 hours (range: 48–120 h), with three participants having stays of 5 days.

NeuraGen Nerve Wrap (NeuraWrap)

NeuraWrap Nerve Protector (Integra LifeSciences Corporation, Plainsboro, N.J.) is an absorbable collagen implant that provides a non-constricting encasement for injured peripheral nerves for protection of the neural environment. NeuraWrap is designed to be an interface between the nerve and the surrounding tissue, when hydrated, NeuraWrap is a pliable, nonfriable, porous collagen conduit with a longitudinal slit that allows NeuraWrap to be spread open for placement over the injured nerve. NeuraWrap is sterile, non-pyrogenic, for single use only. The device is cleared through the FDA's 510(k) process (K041620).

At this time, the available peer-reviewed published data addressing the clinical utility of NeuraWrap is limited to a small number of studies (Hibner, 2012; Kokkalis, 2016; Soltani, 2014). Additional evidence addressing the clinical utility of this product from large, well-designed, and conducted trials is needed to fully assess the clinical utility of this product.

NovoSorb Biodegradable Temporizing Matrix (BMT)

NovoSorb Biodegradable Temporizing Matrix (BMT) (PolyNovo Biomaterials Pty Ltd., Victoria, AU) is composed of porous biodegradable polyurethane foam bonded with a polyurethane adhesive layer to a fenestrated one-sided

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transparent sealing membrane. The sealing membrane is designed to physiologically close the wound by limiting evaporative water loss during integration of the foam. The adhesive layer and sealing membrane are to be removed and discarded when appropriate leaving only the foam layer to biodegrade. NovoSorb is indicated for use in the management of wounds including: partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic and vascular ulcers, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) and draining wounds. The device is for single use only. NovoSorb is cleared through the FDA's 510(k) process (K172140).

At this time there is a reasonable number of studies published in the medical literature addressing the use of NovoSorb for a variety of conditions including burns, treatment of necrotizing fasciitis, DFUs, and chronic complex wounds (Solanki, 2020; Schlottmann, 2022; Li, 2021; Lo, 2022; Austin, 2023; Kidd, 2023; Lo, 2023; Betar, 2023; and Guerrico, 2023). However, due to several factors, including a nongeneralizable sample and other factors, the results cannot be generalized to the wider population. Larger studies in the form of well-designed and conducted trials are needed to assess the clinical utility and efficacy of NovoSorb.

ologen Collagen Matrix

ologen Collagen Matrix (Aeon Astron Europe B.V., Leiden, CH) is a biodegradable material composed of collagen obtained from porcine collagen and glycosaminoglycans (GAG). The device is gamma sterilized for single use only. ologen Collagen Matrix is intended for the management of wounds including surgical wounds, trauma wounds, draining wounds, second degree burns, partial and full-thickness wounds, pressure ulcers, venous ulcers, vascular ulcers, diabetic ulcers, oral wounds and sores. ologen is cleared through the FDA's 510(k) process (K173223). The use of this product has been proposed for a variety of ophthalmological indications.

The most rigorous trial to date was an open label, non-randomized, prospective study involving 93 participants undergoing phacotrabeculectomy assigned to receive treatment with mitomycin C (n=53) or ologen (n=40). The authors reported that after 12 months follow-up there were no significant differences between groups with regard to best corrected visual acuity (p=0.151), intraocular pressure (p=0.254), mean number of medications used (p=0.91) or overall procedure success (p=0.745). No reported repeat procedures, blebitis or endophthalmitis were reported. This study indicates equal outcomes from the use of mitmycin C compared to ologen during phacotrabeculectomy. However, the study was not designed as a non-inferiority trial and contained several methodological flaws that limit the generalizability of the reported findings. Further investigation in the form of well-designed and conducted studies is needed (Chelerkar, 2021).

Park (2022) published a retrospective analysis of 72 individuals with glaucoma who underwent XEN gel stent implantation with (n=42) and without (n=30) ologen collagen matrix augmentation. Surgical success, defined as intraocular pressure (IOP) reduction greater than 20% than preoperative IOP, and the percentage of postoperative complications were compared between the ologen implant augmented group and the non-augmented group. The surgical success rate at 6 months postoperatively was not different between the groups (56.4% compared to 43.3%, p>0.05). Neither was the prevalence of postoperative hypotony, 5-fluorouracil injections, use of anti-glaucoma medications, bleb needling, and additional glaucoma surgeries different between the groups at 6 months. The authors concluded that all groups showed IOP reduction after XEN gel stent implantation, however there was no significant difference between the Ologen implant augmented and non-augmented groups in surgical outcomes.

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Bhatkoti (2023) and Khairy (2023) also published small studies that assessed the use of ologen implant in place of or in combination with trabeculotomy. Bhatoki (n=43) demonstrated a similar success rate between trabeculectomy and ologen implant in treating primary open angle glaucoma. However, there was a lower complication rate and faster visual recovery in the trabeculectomy-only group compared to the ologen group. Khairy (n=21) compared the use of Mitomycin C or ologen implant as an adjunct to combined trabeculotomy-trabeculectomy in the treatment of primary congenital glaucoma. Complete success was achieved in 17 eyes (81.0%) in combined trabeculotomy-trabeculectomy group, 18 eyes (85.7%) in Mitomycin-C group, and 17 eyes (81.0%) in the ologen group. Qualified success, defined as IOP < 21 with or without antiglaucoma medications, was achieved in 85.7% in both the combined trabeculotomy-trabeculectomy and the ologen groups, and 90.5% in the Mitomycin C group. The ologen group had the lowest success probability at 3 months (85.7%). The authors concluded that combined trabeculotomy-trabeculectomy is a safe and effective primary surgical treatment in individuals with primary congenital glaucoma without the need for implant augmentation, and that the use of ologen implant should be preserved for use in recurrent cases. Additional larger studies are needed to assess the safety and clinical efficacy of ologen in ophthalmic applications.

Pelvicol

Pelvicol is a porcine-derived acellular dermal collagen intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes. It is specifically indicated for plastic and reconstruct surgery of the face and head. It is cleared through the FDA's 510(k) process (K013625).

The use of Pelvicol was evaluated in 132 participants with pelvic organ prolapse. This RCT involved 64 participants who underwent anterior and posterior colporrhaphy and 68 who received colporrhaphy with Pelvicol. At 3 months follow-up, there were significantly more surgical failures and recurrences in the Pelvicol group, but by the 3-year follow-up period recurrence rates were similar. No significant differences were noted with regard to symptom resolution, sexual activity, or complications rates. The authors conclude that, "Pelvicol did not provide advantages over conventional colporrhaphy in recurrent pelvic organ prolapse concerning anatomical and subjective outcomes."

Kahn (2015) published the results of an RCT involving 201 participants undergoing surgical treatment for stress urinary incontinence. Participants received treatment with either tension-free vaginal tape (TVT), autologous fascial sling (AFS), or Pelvicol. The authors reported that 162 (80.6%) participants were available for follow-up at a median follow-up of 10 years. They reported the 1 year "success rates", defined as being completely dry or improved, as 93% in the TVT group, 90% in the AFS group and 61% in the Pelvicol group. There were no significant differences between groups at 10 years. Comparing the 1- and 10-year success rates, there were significant reductions in the TVT and AFS groups ($p<0.05$ for both), but not for the Pelvicol group ($p=1.0$). Similar results were reported with the rates of "dry" participants at 1 and 10 years, with rates for TVT reported as being 55% and 31.7%, 48% and 50.8% for AFS, and 22% and 15.7% for Pelvicol. These rates significantly favored AFS ($p<0.001$ vs. Pelvicol and $p=0.001$ vs. TVT). The Pelvicol arm of the study was discontinued by the data monitoring group after it was clear that the Pelvicol group had significantly poorer results compared to TVT and AFS. The results of this study indicate that the use of Pelvicol for the treatment of stress urinary incontinence may present a significant risk of harm compared to other available treatments, and further investigation may be warranted.

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Peri-Strips Dry

Peri-Strips Dry (Bio-Vascular, Inc. St. Paul, MN) is a surgical mesh product derived from decellularized bovine pericardium that is crosslinked with glutaraldehyde. Peri-Strips Dry is indicated to reinforce staple lines during lung and bronchus resections including: wedge resections, blebectomies, lobectomies, bullectomies, bronchial resections and other lung incisions and excision of lung and bronchus. It can also be used for the reinforcement of the gastric staple line during bariatric surgical procedures and gastric bypass and gastric banding. Per-Strips Dry is cleared through the FDA's 510(k) process (K971048).

At this time there are only a limited number of peer-reviewed published articles addressing the use of this product. Stamou compared the use of Peri-Strips Dry (n=96) to standard care (n=91) in staple line reinforcement during sleeve gastrectomy procedures (2011). The authors reported that the use of Peri-Strips Dry significantly reduced the incidence of staple line bleeding (p=0.012) and intra-abdominal collections (p=0.026), however, the leak rate was not significantly reduced.

A similar study was conducted by Shah and others (2014) involving 100 participants undergoing sleeve gastrectomy procedures and assigned to surgery with either Peri-Strips Dry staple line reinforcement (n=51) or standard care (n=49). Participants were followed up for 30 days post procedure. No intra- or postoperative leaks were reported in either group. Staple line bleeds were reported to occur less in the Peri-Strips group compared to controls (45.1% vs. 79.6%, p=0.0005). Overall BMI did not impact staple line bleeds ($p_{interaction}$=0.072). However, participants with BMI < 43 were significantly more likely to have staple line bleeds compared to participants with BMI ≥ 43 (79.3% vs. 33%, p=0.0015). Participants in the Peri-Strips group had less severe staple line bleeding compared to controls, with moderate to severe bleeding occurring in 2 Peri-Strips group participants compared to 6 controls (p=0.0002). Peri-Strips participants also had shorter procedure times (58.8 minutes vs. 72.8 minutes, p=0.0153) as well as fewer hemostatic clips or sutures (19.6% vs. 67.3%, p<0.0001).

Permacol

Permacol Surgical Mesh (Tissue Science laboratories, PLC. Hants, UK) is an acellular dermal collagen product derived from porcine pericardium and elastin. Permacol is intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes. It is specifically indicated for use in the following types of soft tissue repair procedures: abdominal, inguinal, diaphragmatic, femoral, scrotal, umbilical, and incisional hernia, colon, rectal, urethral and vaginal prolapse, muscle flap reinforcement, reconstruction of the pelvic floor, sacrocolsuspension, and urethral sling. Permacol is cleared through the FDA's 510(k) process (K992556).

Mitchell (2008) published a retrospective, nonrandomized controlled study of 37 participants undergoing congenital diaphragmatic hernia repair. Participants received treatment with either Permacol (n=29) or synthetic Gore-Tex (n=8), with a median follow-up of 57 months for Gore-Tex and 20 months for Permacol. Overall recurrences were reported in 8 (28%) Gore-Tex participants with a median time to recurrence of 12 months. There were no recurrences reported in the Permacol group. These results are interesting, but due to the small sample size, retrospective nature and lack of randomization, it is not possible to generalize the results to other populations.

Kalaiselvan (2020) performed a retrospective analysis of 13 participants who had abdominal wall defect repair with bridging Permacol over a 5-year period. Twelve of these (92%) participants developed abdominal wall defects

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(AWD) and enterocutaneous fistulation following complications of previous surgery. Six participants underwent fistula takedown and abdominal wall repair with Permacol, of which 5 (83%) recurred. Seven participants had already undergone similar procedures in their referring hospitals and had also recurred. Median time to fistulation after Permacol treatment was 17 days. In all cases, Permacol was used to bridge the defect and placed in direct contact with bowel. At reconstructive surgery for refistulation, it was inseparable from multiple segments of small intestine, necessitating extensive bowel resection. Histological examination confirmed that Permacol almost completely integrated with the seromuscular layer of the small intestine. The study raised concerns regarding intraperitoneal use due to the fact that Permacol may become inseparable from the serosa of the small intestine and was associated with recurrent intestinal fistula formation and treatment failure.

Rashid (2020) examined rotator cuff repair augmented with either GraftJacket (n=4), Permacol (n=3) or SOC (n=3). The study addressed histological and proinflammatory changes in the native supraspinatus tendon in both Permacol groups. The authors reported increased friability of the matrix, and lack of parallel oriented collagen fibers. In the SOC group, which was a conventional repair without patch augmentation, the tissue resembled normal tendon. The Permacol-treated sections, however, demonstrated more disruption of the extracellular matrix when compared to sections treated with GraftJacket. They reported that one participant in the Permacol group experienced adverse tissue reaction characterized by extensive infiltration of pro-inflammatory cells. The authors concluded use of Permacol augmentation in rotator cuff repair lacks clinical efficacy and may potentially cause harm.

Roman (2021) reported the results of a retrospective case-control study of 209 participants undergoing complete excision of large rectovaginal endometriotic nodules treated with (n=167) or without Permacol (n=42) mesh. No significant differences were reported in the rate of postoperative rectovaginal fistula formation (OR, 1.6) and the authors concluded that the use of Permacol mesh may not impact the rate of rectovaginal fistula formation compared to no mesh.

Vahtsevanos (2021) reported the results of a retrospective case-control study of 73 participants who had undergone 76 parotidectomy procedures with (n=32) and without Permacol (n=44) to evaluate the impact on the incidence of Frey's syndrome. At a mean follow-up of 26.3 months the incidence of Frey's syndrome was significantly lower in the Permacol group (6.7% vs. 31.8%, respectively, p=0.031). The incidence of severe Frey's syndrome was 3.12% in the Permacol group compared to 31.82% in the control group (p=0.002). The results of this study should be confirmed in a prospective trial.

Ball (2022) conducted a parallel, dual-arm, double-blind randomized controlled trial involving adults (n=94) undergoing complex abdominal wall reconstruction with a biologic mesh (2017–2020). Participants were randomized in a 1:1 ratio to receive either Strattice or Permacol biologic meshes. The incidence of complications between groups was not statistically significant (46.0% vs. 64.6%; p=0.06). A total of 14 (14.9%) participants experienced a hernia recurrence, with no differences between groups (n=6 in the Permacol group and n=8 in the Strattice group).

Promogran

Promogran Matrix Wound Dressing is a sterile primary dressing comprised of (Johnson & Johnson Medical, Ltd., North Yorkshire, UK) is an acellular dermal collagen product of bovine origin. Program is indicated for the management of exuding wounds including, diabetic foot ulcers, venous ulcers, ulcers caused by mixed vascular

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etiologies, full thickness and partial thickness wounds, donor sites and other bleeding surface wounds, abrasion, traumatic wounds healing by secondary intention, and dehisced surgical wounds. Promogran is cleared through the FDA's 510(k) process (K014129).

The use of Promogran has been evaluated in two RCTs. The first, by Veves and others, involved 276 participants with DFUs randomized to receive treatment with either Promogran (n=138) or moistened gauze (control group; n=138) (2002). At 12 weeks of treatment, there was no statistically significant difference between groups with regard to complete wound closure (p=0.12), in healing for either the subgroup of participants with wounds of less than 6 months duration (p=0.056), or the group with wounds of at least 6 months duration (p=0.83). No differences were seen in the safety measurements between groups. The other study by Vin involved 73 participants with VSUs randomly allocated to receive either Promogran (n=37) or a non-adherent dressing (Adaptic) (n=36). Only 29 participants completed the 12-week study period (39.7%). No intent-to-treat analysis was provided. Because of this, the data reported is not particularly useful.

PuraPly

PuraPly antimicrobial wound matrix is an acellular dermal collagen product composed of a purified collagen matrix of bovine origin containing polyhexamethylenebiguanide (PHMB). PuraPly AM is intended for the management of wounds and as an effective barrier to resist microbial colonization within the dressing and reduce microbes penetrating through the dressing. PluraPly may be used for the management of: partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree bums, and skin tears) and draining wounds. PuraPly is cleared through the FDA's 510(k) process (K051647).

Lintzeris (2018) published a case series involving 8 participants with chronic wounds with a variety of etiologies including trauma (n=1), DFUs (n=1), pressure ulcers (n=3), venous stasis ulcers (VSUs) (n=1), surgical wounds (n=1), and calciphylaxis ulcers (n=1). PuraPly AM was applied once weekly after debridement. The authors reported a mean of 5.8 PuraPly applications were used. A total of 6 wounds had complete healing at an average time to closure of 10 weeks. The 3 wounds that did not completely heal demonstrated improved wound appearance with 100% granulation with an average area reduction of 61.4%.

Bain (2020) published the results of the Real-World Effectiveness Study of PuraPly AM on Wounds (RESPOND) registry, a prospective cohort study involving 307 participants with wounds with a variety of etiologies including VSUs (n=67), DFUs (n=62), pressure ulcers (n=45), surgical wounds (n=54), and other wounds (n=79) treated with PuraPly AM. Participants were followed for 32 weeks. The authors reported the mean number of PuraPly AM applications as 5.2. Full wound closure was 52% at 20 weeks, 62% at 26 weeks, and 73% at 32 weeks. Complete wound closure for VSUs was 73%, for DFUs was 51%, for pressure ulcers 62%, for surgical wounds 96% and 67% for other wounds. No adverse events or serious adverse events attributable to PuraPly were reported.

Koullias and others (2022) completed a secondary analysis of the RESPOND registry examining the effects of PuraPly AM treatment in the subgroup of participants with VSUs (n=67) over 32 weeks. The use of PuraPly resulted in successful healing defined as > 60% reduction from baseline in wound area and depth, as well as the incidence of wounds demonstrating > 75% reduction from baseline in wound volume. This resulted in successful

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healing in 73% of participants as demonstrated by reduction in area, depth, and volume. A limitation of the study was the participants included were predominantly white (87%) females (58%).

Menack (2022) also completed a secondary analysis of the RESPOND registry in a subgroup of participants with pressure injuries (PI) (n=45). The participants were primarily elderly, with large deep wounds of long duration. The use of PHMB in the management of PI resulted in 91% PAR and 62% rate of healing.

Regeneten

Regeneten (Rotation Medical, Inc. Plymouth, MN) is an acellular dermal collagen product composed of bovine collagen. Regenten is indicated for the management and protection of tendon injuries in which there has been no substantial loss of tendon tissue. It has been cleared through the FDA's 510(k) process (K222501).

Clinical use of the Regeneten graft has been described in several studies. The first, published by Bokor and others (2016) described a case series study of 13 participants with intermediate- to high-grade partial thickness rotator cuff tears who were followed for 2 years. At the end of the study 10 participants with evaluable tears had demonstrable improvement in tear appearance on MRI, with 7 completely healed. The remaining 3 participants had continued tears, but with continued improvement. No evidence of tear progression was reported. Clinical symptoms were shown to improve significantly in overall Constant-Murley shoulder scores ($p \leq 0.01$) and Constant-Murley pain score, ($p \leq 0.001$), as well as American Shoulder and Elbow Society (ASES) total score ($p \leq 0.001$), and ASES pain score ($p \leq 0.001$). No postoperative infections and no adverse events associated with the product were reported.

Schlegel reported the results of a prospective case series study involving 33 participants with intermediate-grade or high-grade partial-thickness tears of the supraspinatus tendon treated with Regeneten and followed for 1 year. Intermediate-grade tears were reported in 12 participants and or high-grade tears in 21. Of these, 11 were articular, 10 were bursal, 4 were intrasubstance, and 8 were hybrid). At 12 months, a total of 8 participants (24%) had no visible defect on MRI, 23 participants (70%) had a decrease in tear size by at least 1 grade. Only 1 participant (3%) had a tear that remained unchanged. No tears progressed to full-thickness tears in the participants who followed the postoperative rehabilitation protocol. No revision procedures were reported. Overall, tendon thickness increased significantly ($p<0.0001$) based upon MRI evidence of new tissue growth over the bursal surface of the supraspinatus tendon. The ASES pain score improved significantly at 1 year, as did the ASES shoulder function score and ASES shoulder index score ($p<0.001$ for all). No device-related significant adverse events were reported.

McIntyre (2019) published the results of a retrospective case series study involving data from participants with partial- and full-thickness cuff tears treated with Regeneten reported in the REBUILD registry. The registry included 203 participants and 173 (85%) had complete 1 year follow-up data. Overall, 90 participants had partial-thickness tears and 83 had full-thickness tears. Of the partial tear group, 16.7% were grade I tears, 37.8% grade II, and 45.5% grade III. Of the full-thickness tears, 4.8% were small, 50.6% medium, 30.1% large, and 14.5% massive. Other surgical procedures were conducted in conjunction with the graft placement, including acromioplasty (89.0%), acromioclavicular joint resection (39.9%), capsular release (12.1%), and biceps surgery (55.6%). At 12 months, the partial-thickness group has a statistically significant improvement with regard to outcomes on the single-assessment numeric evaluation (SANE), Veterans RAND 12-Item (VR-12) physical component, ASES, and Western Ontario Rotator Cuff (WORC) measures ($p<0.05$ for all). For the VAS pain and ASES scores, improvement was 84% and 83%, respectively, which met or exceeded each measure's minimal clinically important difference (MCID). In the full-thickness group, a statistically significant improvement was

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reported at the 12 month point on the VAS, SANE, VR12 physical component, ASES, and WORC measures ($p<0.05$ for all). MCIDs were met or exceeded on the VAS and ASES tools in 72% and 77% of participants, respectively. Revision surgery for complications was required in 8 participants (4.6%). Indications included progression of a partial thickness tear to a full thickness tear, deep vein thrombosis and adhesive capsulitis, loose mobile graft remnant in the joint, recurrent effusions, and failure to heal. In the partial thickness group, 29 participants (32.2%) required corticosteroid injections in the postoperative period for pain control, and 9 participants (10.8%) in the full-thickness group required injections. The majority of post-operative steroid injections administered in the study were done in 2 centers accounting for 76% of injections. Nine sites did not administer any steroid injections.

Thon (2019) reported on the results of a prospective case series study of 23 participants with large (n=11) or massive (n=12) full-thickness rotator cuff tears treated with Regeneten. In addition to complete rotator cuff repair, participants underwent subacromial decompression (n=19), distal clavicle excision (n=17), biceps tenodesis/tenotomy (n=12), and suprascapular nerve release (n=5). Mean time to postoperative MRI was 13 months, and the final ultrasound evaluation was 24 months. Complete healing on both measurements was reported to be 96%, with 2 treatment failures. No difference was found between the two tear groups with regard to final ASES scores ($p=0.69$). There were no postoperative infections or adverse events associated with the device.

The results of these studies are all promising, but the methodology used limit the generalizability of this data to larger populations. Additional studies are warranted to better understand the clinical utility of Regeneten for rotator cuff repair surgery.

Seamguard

Seamguard (W.L. Gore and Associated, Flagstaff, AZ) is a synthetic product composed of polytetrafluroethylene. The device is intended for use as a prosthesis for surgical repair of soft tissue deficiencies using linear surgical staplers. The device can be used to reinforce staple lines during lung resections, abdominal and thoracic wall repairs, gastric banding, muscle flap reinforcement, rectal and vaginal prolapse, pelvic floor reconstructions, urethral sling, and diaphragmatic, femoral, incision, inguinal, lumbar, paracolostomy, scrotal and umbilical hernias. Seamguard is cleared through the FDA's 510(k) process (K955364).

Salgado (2011) published a randomized controlled trial evaluating the use of Seamguard compared to extraluminal suturing or fibrin glue for open bariatric surgical procedures (2011). Twenty participants were assigned to each group; however, enrollment in the fibrin glue group was stopped due to serious complications, including leaks requiring surgical intervention. The authors report that no significant differences were found between the Seamguard group and the suturing group. This study was not designed or powered to be a non-inferiority study, so these findings are not particularly useful in understanding the safety and efficacy of Seamguard.

Albanopoulos (2012) published a study comparing Seamguard to staple line suturing in laparoscopic sleeve gastrectomy procedures. This study enrolled 90 participants, 48 who were assigned to the Seamguard group and 42 to the suturing group. As with the Salgado study, the authors reported no significant differences in measured outcomes. One exception to this was a 6.2% complication rate in the Seamguard group compared to no complications in the suturing group.

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In 2013, Wallace published the results of a nonrandomized controlled study of 36 participants undergoing pancreatectomy with the addition of Seamguard to the stapled stump closure. This group was compared to 18 historical controls undergoing the same procedure without Seamguard. Postoperative leak rate was reported in 8% in the experimental group compared to 39% in the control group. This study is limited due to its small population, use of historical controls and other methodological issues.

Guerrier and others (2018) published the results of a retrospective review of 256 participants undergoing laparoscopic sleeve gastrectomy. Participants received treatment with staple line reinforcement with oversewing (n=28), reinforcement with Seamguard (n=115), or no staple line reinforcement (n=111). Intraoperative staple line bleeding was significantly reduced in the reinforcement group (22.3 vs. 37.8%, p=0.003). Gastric leaks were reported in 9 participants (3.52%), with no difference between any reinforcement method (2.7 vs. 2.1%, p=0.54). The authors did note that oversewing of the staple line was associated with higher incidence of stenosis, a serious complication with significant morbidity and mortality ($p<0.01$). The authors concluded that their study demonstrated that staple line reinforcement does not provide significant leak reduction but does reduce intraoperative staple line bleeding. However, this must be viewed in light of the increased risk of stenosis development.

In a 5-year, single-center retrospective case-control study, Vitiello (2024) analyzed 626 individuals undergoing laparoscopic sleeve gastrectomy, comparing 450 procedures reinforced with GORE SeamGuard to 176 procedures without any staple line reinforcement. The no-reinforcement group experienced a 2.26% rate of leaks or bleeding, whereas the GORE SeamGuard group recorded 0% staple line complications ($p<0.05$). In addition, 13 external cases of staple line complications treated at the same center all involved laparoscopic sleeve gastrectomy performed without reinforcement.

STRAVIX

STRAVIX (Smith & Nephew, Andover, MA) is a cryopreserved allogeneic umbilical cord tissue product regulated by the FDA through the HCT/P pathway and designed to treat large, post-operative diabetic foot wounds with exposed tendon, muscle, or bone.

In a single-blind, 12-week randomized trial by Lavery (2024), 40 individuals with foot wounds classified as categories 2A through 2D or 3A through 3D in the University of Texas Wound Classification were assigned to receive either the cryopreserved version (Stravix) or a lyopreserved version at baseline and again after 4 weeks. After 12 weeks, wound closure was observed in 36.8% of the cryopreserved group and 19.0% of the lyopreserved group (p=0.21); infection rates were 10.5% and 4.8%, respectively (p=0.60). Mean reductions in wound area (75.9 ± 32.3% vs. 65.5 ± 38.4%, p=0.41) and wound volume (85.0 ± 30.8% vs. 79.9 ± 31.9%, p=0.61) were also not significantly different. Overall, infections were noted in approximately 7.5% of participants, which was lower than anticipated for this high-risk population. This study indicates no significant differences in clinical performance between a cryopreserved version or a lyopreserved version of Stravix. However, it is not clear how these products perform against other more widely used products.

Suprathel

Suprathel is a synthetic copolymer consisting mainly of DL-lactide (>70%), trimethylenecarbonate, and e-caprolactone and was cleared under the FDA's HTC/P process.

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An RCT involving 22 participants with burn injuries treated with STSG was reported by Schwarze in 2007. Each donor site was randomly selected and was treated with Suprathel or Jelonet. There was no significant difference between the two materials tested regarding healing time and re-epithelization, but a significantly lower pain score was reported for the participants treated with Suprathel (p=0.0002). The same group reported the results of another RCT study involving 30 participants with burn injuries (Schwarze, 2008). Wounds from each participant were randomly selected and partly treated with Omniderm and partly treated with Suprathel. There was no significant difference between the two products regarding healing time and re-epithelization. There was a significantly lower pain score for participants treated with Suprathel (p=0.0072).

Rashaan (2017) reported the use of Suprathel in a population of 21 children with partial thickness burns. The authors reported a median reepithelialization time of 13 days (range 7-29), and 3 participants required treatment with split skin grafts. There were 7 (33%) participants with wound colonization before application of Suprathel, which increased to 12 (57%) during treatment. Only 1 participant developed a wound infection.

Nischwitz (2021) published the results of a prospective case series study involving 22 participants with chronic leg wounds treated with Suprathel and followed for 8 weeks. Out of the original participant pool, 19 participants completed the trial. No significant difference in average wound size was reported between baseline and 4 weeks (p=0.074). The wound size changed significantly between 4 and 8 weeks (p=0.031). Overall, the average wound size between baseline and 8 weeks decreased significantly (p=0.006). One wound was reported as healed at 4 weeks (5.3%) and two at 8 weeks (15.79%). When stratified by wound age < 12 months and > 12 months, the overall wound size had a significant reduction for both old and young wounds (p=0.002 and 0.03, respectively). Similar findings were reported for both diabetic (p=0.014) and non-diabetic wounds (p=0.028). No adverse event associated to the intervention had occurred in the study period.

Heitzmann (2023) published a prospective intra-individual clinical study in 23 individuals with burn injuries aged 18 to 85 years that compared Suprathel and Jelonet in the treatment of deep dermal burns after enzymatic debridement. Individuals had sustained partial-thickness-to-deep-thickness flame, scald, or contact burns of their hands or feet, with more than 0.3% of TBSA. The outcomes measured were wound healing, participant comfort, and pain. Wounds were divided in 2 areas, one treated with Suprathel and the other with Jelonet. Suprathel was placed on the wounds and gradually cut back as the re-epithelialization progressed until the dressings were completely detached. The Jelonet dressings were changed every 2 days. Wound closure was documented with a mean of 18.44 days for wounds treated with Suprathel, and 18.81 days with Jelonet (p=0.58), with no significant difference in final wound healing time, only 1 individual had a second debridement followed by skin grafting. Less pain was reported during the dressing changes with Suprathel compared to Jelonet on day 2 (p<0.001) and day 4 (p<0.0). Additionally, the wound areas treated with Suprathel showed less exudation and bleeding. The authors concluded that both dressings achieve safe and rapid healing after the enzymatic debridement of deep dermal burns of the hands and feet. However, the results of this study require further investigation in the form of more robust and well-designed trials.

Karlsson (2023) reported a retrospective, single center study of 58 pediatric individuals with burns comparing Suprathel (n=30) to Mepilex® Ag (n=28). The outcomes measured were healing time, burn wound infection, need for operations and number of dressing changes. The results showed that healing within 14 days occurred in 17 Suprathel group participants and 15 in Mepilex Ag group participants. A total of 10 participants from each group received antibiotics for suspected burn wound infection, and 2 from each group had skin grafting. The median

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number of dressing changes was 4 in each group. The authors concluded that the results were similar with both Suprathel and Mepilex Ag dressings. However, they noted that these results to be interpreted with caution due to the retrospective study design, and the fact that burns were significantly larger in the Mepilex Ag group.

In a randomized controlled trial involving 40 individuals undergoing split-thickness skin graft procedures for non-melanoma skin cancer, donor sites were dressed in either Suprathel or Hypafix adhesive tape (Cussons, 2024). Of the original 40 participants, only 16/20 (80%) of participants in the Suprathel group and 14/20 (70%) in the Hypafix group completed the trial, resulting in a loss to follow-up of 70% . The results showed no statistically significant difference in mean time to healing (31.7 vs. 27.3 days, p=0.182), pain, itch, or final scar outcomes at 13 weeks, as measured by the Patient and Observer Scar Assessment Scale. Neither group had postoperative infections. Although these findings suggest that Suprathel may not provide clear advantages for older individuals with small-area donor sites, the trial's methodological limitations prevent further conclusions. Further high-quality research with larger populations is warranted.

In a retrospective, single-center study by Delgado-Miguel (2024) involving 378 individuals under 18 years old, three skin substitutes (Suprathel [n=92], EZ-derm [n=179], and Biobrane [n=107]) were compared for short- and long-term outcomes in pediatric partial-thickness burns. Although the groups had similar demographics and burn characteristics, the Suprathel group exhibited a significantly shorter median hospital stay ($p<0.01$), lower escharectomy and grafting rates (p=0.018), and fewer long-term reoperations (p=0.031). No differences in long-term complications were observed between groups. While these findings suggest Suprathel may offer distinct advantages, the single-center, retrospective study design may limit generalizability. Further high-quality, multicenter research is warranted.

SURGISIS Biodesign Tissue Graft **(also known as Biodesign)**

SURGISIS Biodesign Tissue Graft (Cook Biotech Inc., West Lafayette, IN), is a product composed of decellularized intestinal porcine mucosa. SURGISIS is intended to be implanted to reinforce soft tissues where weakness exists, and is purported to minimize tissue attachment to the device in cases of direct contact with viscera. Several forms of Surgisis/Biodesign are available, including Anal Fistula Plug (AFP), 4-Layer Tissue Graft, Dural Graft, Hernia Graft, and others. Cook Medical, the manufacturer of this product changed the name of Surgisis products to Biodesign in 2008. However, the medical literature continues to refer to these products by their former name. Indications for use include the repair of a hernia or body wall defect. SURGISIS is cleared under the FDA's 510(k) process (K073391).

At this time, there are a large number of case series studies published on the use of the Surgisis anal fistula plug (AFP) (Champagne, 2006; Cintron, 2013; Ellis, 2010; Ky, 2008; O'Connor, 2006; Schwandner, 2009; Thekkinkattil, 2009). The vast majority of these involve very small sample sizes and short follow-up times. The uncontrolled nature of these studies minimizes the scientific value of this data.

Several RCTs are currently available addressing the use of Surgisis for the treatment of anal fistulae. The first study, reported by Ortiz et al., involved 43 participants randomized to receive either endorectal advancement flap surgery or insertion of an anal fistula plug (2009). The drop-out rate was greater than 20% for each group. The authors reported that the relative risk for recurrence was 6.4 for those who received the plug intervention during the 1-year follow-up. Additionally, of the 16 who had previous fistula surgery, 9 had recurrence and 8 of these were from the plug group. Overall, the authors concluded that the anal fistula plug was associated with a low rate of

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fistula healing, especially in individuals with a history of fistula surgery. The second study included 60 participants with perianal fistulas who were randomly assigned to receive treatment with Surgisis (n=31) or a mucosal advancement flap (n=29) (van Koperen, 2011). Both participants and investigators were blinded to group assignment. At a follow-up of 11 months, the recurrence rates were 71% (n=22) in the Surgisis group compared to 52% (n=15) in the mucosal advancement flap group, which was not significantly different. Additionally, no significant differences were reported with regard to postoperative pain, pre- and postoperative incontinence scores, soiling, and quality of life. Senéjoux (2016) reported the results of an open-label, randomized controlled trial comparing seton removal alone (n=52) compared to Surgisis (n=54) in 106 participants with Crohn's disease and at least one ano-perineal fistula tract drained for more than 1 month. The authors reported that fistula closure at week 12 was achieved in 31.5% of participants in the Surgisis group compared to 23.1 % in the control group (p=0.19). No interaction in treatment effect was found when data was analyzed to control for case complexity (p=0.45). Adverse events at week 12 were reported in 17 participants in the Surgisis group compared to 8 controls (p=0.07). The authors concluded that the use of Surgisis was not more effective than seton removal alone. In 2017, Bondi and others published the results of an RCT involving 94 participants with cryptogenic trans-sphincteric anal fistulas assigned to treatment with either Surgisis (n=48) or mucosal advancement flap (n=46). The authors reported that the recurrence rate at 12 months was 66% in the Surgisis group and 38% in the flap group (p=0.006). While anal pain was reduced after operation in both groups, anal incontinence did not change in the follow-up period for either. No differences between the groups were reported with regard to pain, incontinence, or quality of life. The authors concluded that there was a considerably higher recurrence rate after the anal fistula plug procedure than following advancement flap repair.

Several studies have reported on the results from nonrandomized controlled, retrospective trials. Ellis described the results of a study that involved 95 control participants who had trans-sphincteric or rectovaginal fistulas repaired via advancement flap repair (2007). The experimental group included only 18 participants who received treatment with Surgisis. The results indicated a significant benefit to the Surgisis procedure. Another study included 80 participants who received treatment with either anal fistula plug or endorectal advancement flap (Christoforidis, 2009). The results of this trial demonstrated that treatment success was close to over twice as likely with the flap procedure compared to treatment with a fistula plug after a mean follow-up period of 56 months. Chung (2009) reported on the results of a retrospective study that involved 245 participants who underwent anal fistula repair surgery with either Surgisis (n=27), fibrin glue (n=23), Seton drain (n=86), or an endorectal advancement flap procedure (n=96). The results indicate that the rate of success was similar between the Surgisis group and the endorectal advancement flap group. Hyman and others conducted a study that involved 245 participants who received one of seven procedures, including the Surgisis plug (n=43), endorectal advancement flap (n=4), Seton drain (n=34), fibrin glue (n=5), fistulotomy (n=156), and other unspecified procedures (n=3) (2009). In contrast to the findings of the Chung study, the authors reported that the Surgisis plug demonstrated the lowest success rate, with only 32% healed at 3 months compared to 87% for the fistulotomy group. In 2014, Blom reported on a case series study involving 126 participants with anal fistulae treated in four different hospitals. After a median of 13 months, 30 (24%) of the fistulae had closed with no discomfort or secretion reported. The outcomes in the four hospitals varied from 13% to 33% with similar numbers of participants in each hospital. A success rate of 12% was observed for participants with anterior fistula compared with 32% for those with posterior tracks [HR for successful healing, 2.98] and 41% for those with a lateral internal opening (HR, 3.76). The authors concluded that their study demonstrated low success rates after the first plug-insertion procedure and that anterior fistulae were much less likely to heal compared with fistulae in other locations.

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Jayne (2019) reported on the results of an RCT involving 304 participants with anal fistula treated with either Surgisis or 'surgeon's choice" (e.g., fistulotomy, cutting seton, advancement flap or ligation of intersphincteric fistula tract [LIFT] procedure). The authors reported clinical evidence of fistula healing in 66 participants (54%) in the Surgisis group compared to 66 participants (55%) in the control group at 12 months. Furthermore, MRI data showed fistula healing in 54 participants (49%) in the Surgisis group compared to 63 participants in the control group. Overall, 12-month clinical healing rates were 55% in the Surgisis group compared to 64%, 75%, 53%, and 42% in the cutting seton, fistulotomy, advancement flap and LIFT procedure groups, respectively. The authors commented that overall, there was no significant difference between the use of Surgisis and other procedures.

A meta-analysis was reported by Lin (2019) that included 11 studies comparing the use of Surgisis to rectal advancement flap (RAF) for anal fistula repair in 810 participants. They reported that the pooled analysis indicated that there was no significant difference between the use of Surgisis and RAF in terms of healing rate, recurrence rate and incidence of fistula complications. However, the pooled results of the 4 RCTS and 1 series study with long-term follow-up revealed that the RAF group had a significantly higher healing rate (OR, 0.32; p=0.01) and lower recurrence rate (OR, 4.45; p=0.009) than the AFP group. These results appear to support the use of RAF over Surgisis for anal fistula repair.

Jayne (2021) published the results of an open-label RCT involving 304 participants undergoing anal fistula repair. Participants were assigned to treatment with either Surgisis anal fistula plug (n=152) or surgeon's preference (advancement flap, cutting seton, fistulotomy, Ligation of the Intersphincteric Fistula Tract procedure, n=152). At 12 months, the authors reported no significant differences between groups with regard to rate of clinical healing (54% in the Surgisis group compared to 55% in the surgeon's preference group, p=0.83). Similar findings were reported with regard to MRI-confirmed healing (49 vs. 57%, respectively, no p-value provided). Additionally, no significant differences between groups were reported at 12 months on the St. Mark's incontinence score (p=0.48), complication rate (23% vs. 20%, p=0.6), or rate of reintervention (23%. vs. 22%, p=0.96). These results indicate that the use of Surgisis is equivalent to other surgical approaches to anal fistula repair.

Unlike the anal fistula plug product discussed above, Surgisis Gold is provided in larger sheets. Sarr and others (2014) conducted an RCT involving 380 participants with body mass index (BMI) ≥ 35 kg/m^2 scheduled to undergo open Roux-en-Y gastric bypass surgery. Participants were randomized to receive standard suture closure alone or Surgisis Gold as a reinforcing adjunct. The authors reported that complications were more common in the Surgisis Gold group with significantly more wound events and seroma formation compared with the suture closure alone group. At final follow-up of 2 years post-procedure, 32 of 185 (17%) participants in the Surgisis Gold group and 38 of 195 (20%) in the control group developed an incisional hernia (p=0.6). Based on these findings, it would seem that the use of Surgisis Gold is not warranted, and further investigation is needed regarding the safety and efficacy of this product.

Korwar (2019) retrospectively reported the treatment of PEH in 154 consecutive participants who underwent standardized laparoscopic suture repair of the hiatus with Surgisis reinforcement. Follow-up barium swallow was performed in 122 participants (79.22%). Symptomatic recurrence was noted in 25 participants (28.73%), and recurrence on barium swallow was noted in 25 participants (20.4%). Both symptomatic and barium swallow recurrence were reported in 10 participants (12.98%). The reoperation rate was 3.25%. The authors concluded that the use of Surgisis Biodesign for PEH repair is safe. They further commented that there was a high recurrence rate in long-term follow-up, but that the majority of recurrences are small, asymptomatic, and the reoperation rate is very low.

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Surgisis Biodesign was also described in the repair of pelvic floor reconstruction following levator abdominoperitoneal excision of the rectum (Thomas, 2019). This retrospective case series study involved 100 participants, for whom 1-, 2-, and 5-year mortality rates were 3, 8 and 12%, respectively. The authors reported that 33 perineal wounds had not healed by 1 month, but no mesh was infected, and no mesh needed to be removed. Only 1 participant developed a symptomatic perineal hernia requiring repair. On review of imaging, an additional 7 asymptomatic perineal hernias were detected. At 4 years the cumulative radiologically detected perineal hernia rate was 8%.

Ravo (2019) described the results of a trial of 104 participants with inguinal hernia repair with a continuous suture of transversalis to transversalis fascia repair reinforced with Surgisis. Long term follow-up was scheduled at 1 week, 1 month, 1 year, 3 years, 7 years, and 10 years, and was achieved in 100%, 100%, 99%, 93%, 89% and 85% of the participants, respectively. The authors reported a recurrence rate of 1.9% (2 participants, one at 1 week in a participant with bilateral IH and one at 7 years). The mean recovery time was 1.2 days (range 1-5 days). Mortality was 0(0%).

In 2021 Alexandridis and others reported the results of a retrospective case series involving 155 participants with pelvic organ prolapse treated with Surgisis. A total of 138 (89.0%) participants completed the 3-month clinical visit, with 12 of the 17 participants not seen being contacted by telephone and included in the analysis of complications. At 3 months, 22 participants (15.9%) had Pelvic Organ Prolapse Qualification system (POP0Q) stage ≥ 2. The overall recurrence rate for Surgisis-treated defects was 11.6%. Reoperations were reported in 13 (8.4%) participants due to prolapse. Additionally, 7 participants experienced prolapse-related symptoms postoperatively, but had no record of reoperation. This data represents a subjective failure rate of 12.9%. Perioperative and postoperative complications occurred in 56% of participants. The most common complications were urinary (n=28) and pain (n=18). Major complications were reported in 8 participants (5.3%). Persistent complications at 3 months were reported in 28% of participants, including vaginal deformations, dyspareunia, stress urinary incontinence, urge urinary incontinence, and pain. Statistical analysis for recurrence identified a significant effect only for previous prolapse surgery at the same compartment as the Surgisis application (p=0.028). Other significant predictors for complications included lower age (p=0.034), smoking (p=0.022) and longer duration of surgery (p=0.003). The authors concluded, “The relatively high recurrence rates do not suggest a clear benefit from SIS graft use.”

Talymed

Talymed (Marine Polymer Technologies, Inc., Danvers, MA) is a synthetic sterile wound matrix product composed of poly-N-acetyl glucosamine (pGIcNAc) isolated from microalgae. Talymed is indicated for the management of wounds including diabetic ulcers, venous ulcers, pressure wound, ulcers caused by mixed vascular etiologies, full thickness and partial thickness wounds, second degree burns, surgical wounds-donor sites/grafts, post-Moh’s surgery, post-laser surgery, and other bleeding surface wounds, abrasions, lacerations, traumatic wounds healing by secondary intention, chronic vascular ulcers, and dehisced surgical wounds. Talymed and is cleared under the FDA’s 510(k) process (K102002).

At this time, only a single RCT is available addressing the use of Talymed (Kelechi, 2011). In this reviewer-blinded trial, 82 participants with VSUs were randomized to receive either standard care (n=20) or to 1 of 3 groups that received standard treatment combined with different treatment frequencies with Talymed: (1) applied only once, (2)

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applied once every other week, or (3) applied once every third week. Seven participants were lost to follow-up, 5 from the 1 application group and 2 from the every 3-week group. Additionally, another 4 participants were withdrawn from the study, 3 from the 1 application group and 1 from the every 3 weeks group. This left 62 participants in the experimental group and 20 in the control group. At 20 weeks, the authors report that 45.0% (n=9 of 20) of participants receiving standard care alone had complete healing, while 45.0% (n=9 of 20), 86.4% (n=19 of 22), and 65.0% (n=13 of 20) of participants receiving Talymed only once, every other week, and every 3 weeks, respectively, had complete healing. This single study is insufficient to allow proper evaluation of the safety and efficacy of Talymed.

TAPESTRY RC Biointegrative Implant

TAPESTRY RC (Zimmer Biomet, Warasaw, IN) is a composite implant composed of poly DL-lactide (PDLLA) and non-crosslinked bovine collagen. It is designed to function as a non-constricting, protective layer between the tendon and surrounding tissues. TAPESTRY is indicated for managing and protecting tendon injuries where there is no significant loss of tendon tissue. The implant was cleared by the FDA through the 510(k) process (K201572).

TIGR Matrix Surgical Mesh

TIGR Matrix Surgical Mesh (Novus Scientific AB, Paradise Valley, AZ) is a synthetic absorbable polymer made of lactide, glycolide, and trimethylene carbonate. It is a surgical mesh for soft tissue repair, including hernia repair. e TIGR is indicated for use in the reinforcement of soft tissue, where weakness exists in individuals undergoing plastic and reconstructive surgery, or for use in procedures involving soft tissue repair, such as for the repair of hernias or other fascial defects that require the addition of a reinforcing material to obtain the desired surgical result. TIGR is cleared under the FDA's 510(k) process (K191749).

Hansson (2020) reported a prospective, single-blind, clinical trial of 24 individuals (n=48 breasts) with bilateral mastectomy and immediate breast reconstruction. Participants were randomized to receive biological Veritas Collagen Matrix on one side and synthetic TIGR Matrix Surgical Mesh on the other side. During the 12-month follow-up the 2 meshes yielded significantly different esthetic results and asymmetry. Due to this finding, recruitment to the study was terminated. No participants were lost to follow-up at 12 months and 24 breasts in each group had an analysis of complications at 1 year postoperatively. All mastectomies were nipple-sparing. The most common complication was seroma formation (38% in the Veritas group compared to 3.8% in the TIGR group, p=0.011). All TIGR meshes were completely integrated during the exchange to a permanent implant, the Veritas meshes were poorly integrated in the participants with seroma. The frequency of total implant loss (stage I + II) in the Veritas mesh group was 8.5% compared to 2% in the TIRG group (p=0.083). There were 2 implant losses and reoperations which were suspected to have been caused by penetration due to thin mastectomy flaps in the same participant. The authors concluded that there is a higher risk for complications, particularly seroma and implant loss, with Veritas compared to TIGR. However, more robust studies with larger sample sizes are needed to confirm these finding with a high degree of certainty.

Paganini (2022) reported the results of a blinded, randomized, prospective trial that compared participant-reported outcomes after immediate breast reconstruction with TIGR mesh and Veritas mesh using the compared materials in the same participant. Twenty-four participants were recruited and all had a prophylactic bilateral mastectomy and a dual-plane reconstruction. There were no capsular contractures in either group at 5 years. No significant differences between groups were reported with regard to reported outcomes. The authors stated that the two products resulted

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in different types of reconstructed breasts, but concluded that the study was limited by its small sample size, varying surgical techniques, and variability in the meshes used, therefore more studies are needed to generalize the findings.

TUTOMESH

TUTOMESH (RTI Biologics, Inc., Alachua, FL) is a bovine pericardium surgical mesh processed with the Tutoplast solvent dehydration process followed by gamma irradiation. TUTOMESH is comprised of collagenous connective tissue with three-dimensional intertwined fibers. Tutomesh is indicated for use in general and plastic surgery applications. These products are intended for repair of pericardial structures and for use as a prosthesis for the surgical repair of soft tissue deficiencies which include: gastric banding, muscle flap reinforcement, rectal and vaginal prolapse, reconstruction of the pelvic floor, and hernias (including diaphragmatic, femoral, incisional, inguinal, lumbar, paracolostomy, scrotal, and umbilical hernias). TUTOMESH is cleared under the FDA's 510(k) process (K081538).

A retrospective review with 41 participants who underwent 52 breast reconstructions using ADMs was reported by Paprottka (2017). Participants received treatment with either EpiFlex (not available in the US, n=15), Strattice (n=21), or Tutomesh (n=16). Follow-up was 36 months (range 12-54). Overall complication rate was 17%, and 7% for the EpiFlex group, 14% for the Strattice group, and 31% for the Tutomesh group. Capsular contracture occurred in 6%, more frequently in this study compared to the current literature. The authors recommended the use of human derived grafting materials (EpiFlex) over those from porcine of bovine sources.

Eichler (2017) published a retrospective, nonrandomized comparative trial involving 54 participants undergoing breast reconstruction procedures using either SurgiMend (n=18) or Tutomesh (n=27) (Eichler, 2017). No difference in complications rates was noted, consistent with other previous reports.

Vascu-Guard

Vascu-Guard is a decellularized product derived from bovine pericardium cleared under the FDA's 510(k) process. Please see the section for Gore® Acuseal Cardiovascular Patch above.

Veritas® Collagen Matrix

Veritas is an implantable surgical patch comprised of decellularized bovine pericardium, it is purported to minimize tissue attachment to the device in cases of direct contact with the viscera. Veritas is intended for use as an implant for the surgical repair of soft tissue deficiencies; this includes but is not limited to the following: buttressing and reinforcing staple lines during lung resection, and other incision and excision of the lung and bronchus, reinforcement of the gastric staple line during the bariatric surgical procedures, and gastric banding, abdominal and thoracic wall repair, muscle flap reinforcement, rectal prolapse excluding rectocele, reconstruction of the pelvic floor excluding transvaginal organ prolapse repair, and repair of hernia. Veritas is cleared under the FDA's 510(k) process (K06295).

Guerette (2009) published an RCT of 94 participants assigned to treatment with either anterior colporrhaphy alone compared to colporrhaphy reinforced with Veritas bovine pericardium graft. This study had significant loss to

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follow-up, with only 72 of 94 (76.6%) participants at the 1-year time point and 59 of 92 (64.1%) at the completion of the study at 2 years. The authors report no significant differences between groups.

Quah (2019) published the results of a retrospective, non-randomized controlled trial involving 215 participants undergoing mastectomy and implant-based reconstruction procedures with either Veritas (n=36) or TiLOOP® Bra (n=179), a product not currently approved for use in the U.S. In the Veritas group, 22 participants underwent unilateral procedures and 7 underwent bilateral procedures. In the TiLOOP group 61 participants underwent unilateral procedures and 59 participants underwent bilateral procedures. The authors reported that the Veritas group had a higher rate of postoperative complications when compared with the TiLOOP group (54% vs. 14%, respectively; p<0.01). This included higher rates of seroma (51.4% vs. 1.7%, p<0.01), nonintegration of mesh (51.4% vs. 1.6%, p<0.01), implant rotation (16.2% vs. 1.6%, p<0.01), infection (18.9% vs. 2.1%, p<0.01), and wound breakdown (10.8% vs. 0.5%, p<0.01). Additionally, when compared to the TiLOOP group, the Veritas group also had a higher rate of major interventions (35.1% vs. 7.8%, p<0.01), minor interventions (18.9% vs. 2.2%, p<0.01), implant loss (8.1 vs. 1.7%, p=0.05), and unplanned return to theater (27% vs. 6.1%, p<0.01). The results of this trial indicate that Veritas, at least when compared to TiLOOP Bra, results in significantly poorer outcomes.

VersaWrap Tendon Protector

VersaWrap (Alafair Biosciences, Inc., Austin, TX) is an absorbable implant device designed to serve as an interface between the tendon and tendon sheath or the surrounding tissues, which provides a non-constricting, protective encasement for injured tendons. VersaWrap is a plant-based surgical mesh composed of hyaluronic acid and alginate. The product can be applied as a sheet or a gel, creating a gliding interface to reduce friction and minimize postoperative complications like tethering. VersaWrap is indicated for the management and protection of tendon injuries in which there has been no substantial loss of tendon tissue. VersaWrap received FDA clearance through the 510(k) process (K160364).

Hones (2023) conducted a single-center retrospective review assessing VersaWrap's effectiveness as a nerve protector during surgical decompression and neurolysis for recurrent compressive neuropathies in the upper extremity. The study involved 20 individuals with recurrent carpal tunnel syndrome (n=5), cubital tunnel syndrome (n=14), and radial tunnel syndrome (n=1). With an average follow-up of 139 days, all participants had previously undergone surgery at the same site, and symptoms had persisted for an average of 2 years before revision surgery with VersaWrap. Postoperative assessments included two-point discrimination, range of motion, muscle power, and standardized scores like DASH and VAS. No intraoperative complications or further revision surgeries were reported. Results showed mean DASH scores of 54.0 (cubital), 66.2 (carpal), and 68.3 (radial), and VAS scores of 2.7, 4.2, and 3.0, respectively. The authors concluded that VersaWrap was a safe and effective nerve protector, though the study was limited by its small size and non-comparative design. Postoperative outcomes measures included static and moving two-point discrimination, range of motion (ROM), muscle power and standardized scores including the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire and Visual Analog Scale (VAS). No intraoperative complications or further revision surgeries were reported. Results showed mean DASH scores of 54.0 (cubital), 66.2 (carpal), and 68.3 (radial), and VAS scores of 2.7, 4.2, and 3.0, respectively. The authors concluded that VersaWrap is a safe and effective nerve protector.

VIA Disc NP

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VIA Disc is a processed human nucleus pulposus tissue allograft treated as human tissue for transplantation under the FDA's HCT/P process.

Beall (2021) reported the results of the VAST RCT involving 218 participants with single- or two-level degenerative disc disease assigned to treatment with either saline injection (n=39), conservative care (n=39), or VIA Disc (n=140). A total of 36 participants (17%) were lost to follow-up or had withdrawn from the study by the 12 month follow-up point (n=7 [18%] saline group, n=12 [30%] conservative group, and n=17 [12%] VIA Disc group), leaving 182 participants completing the trial. There were 58 participants treated at least one intravertebral level outside of the predefined levels of degeneration for inclusion. Younger participants were reported to have had a more favorable outcome vs. older participants in regard to improvement in Oswestry Disability Index (ODI) for participants less than the median age (32 years old, p=0.004). Clinically meaningful improvements were observed in the VIA Disc group, with a mean reduction in ODI of 27 at 12 months (no p-value provided). ODI-based function was noted to have worsened in the conservative care group during the first 3 months and all participants in this group crossed over to the VIA Disc group in an unblinded fashion. Results for both VIA Disc groups were similar at 12 months. Mean pain reduction as represented by change in Visual Analog Scale of Pain Intensity (VASPI) at 12 months was reported to be 30.5, 34.0, and 46.7 for the saline, VIA Disc, and conservative/crossover groups, respectively. Mean functional improvement per ODI was 23.9, 27.4, and 36.5 respectively (no p-values provided). No differences between participants treated at a single compared to two levels were noted. A modified intention-to-treat analysis indicated significant differences between the VIA Disc compared to saline groups, with a ≥ 15-point reduction in ODI measures (p=0.030). No significant differences were found between groups with regard to the number of participants achieving a 50% reduction in pain at 12 months (p=0.467). In an ad hoc analysis of responders in all groups, participants in the VIA Disc and conservative/crossover groups achieved a statistically significant reduction in pain compared to saline group participants (p=0.022). There were 66 (29.8%) total adverse events in the VIA Disc group compared to 5 (13.2%) in the saline group (no p-value provided). Twenty-three potentially VIA Disc-related events were reported compared to none in the saline or conservative treatment only groups. The conservative/crossover group experienced 7 VIA Disc-related events (8.6% of participants in the crossover group). Most events in the VIA Disc group were musculoskeletal and connective tissue related, with 41 total events (22.0%) and 14 VIA DISC-related events (9.2%). The most common event was pain. In the saline group no adverse events were reported, while the conservative/crossover group reported back pain as a related event in 2.9% of participants.

A total of 11 serious adverse events were reported in the VIA Disc group (3.5%), with 6 considered possibly related to the treatment and/or procedure. Reported events included pain, back pain, bacteremia, and osteomyelitis. No serious events were reported in the saline group or conservative treatment only groups. One serious adverse event (2.6%) was reported in the conservative/crossover group (p=0.832). The 1 SAE in the crossover group was considered not related to treatment or procedure. The results of this trial indicate some potential benefit to the use of VIA Disc, but several methodological flaws limit the generalizability of this trial, including significant loss to follow-up, cross over of a large percentage of the control group to active treatment, loss of blinding, and others.

Hunter (2021) published the results of a post hoc analysis of the VAST trial data exploring it stratified by age. They reported that participants younger than 42 years of age experienced significantly more improvement from treatment with VIS Disc than those older than 42 when compared to those in the saline treatment group. Furthermore, they noted that in participants older than 42 years of age, no differences between groups were seen with regard to functional benefit.

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VICRYL Mesh

VICRYL Mesh (polyglactin 910) Mesh (Ethicon, Inc., Summerville, NJ) is a synthetic absorbable sterile copolymer made from glycolide and L-lactide. VICRYL may be used wherever temporary wound or organ support is required (kidney, liver, spleen), and may be cut to the shape or size desired for each specific application. VICRYL mesh was approved via the FDA's 510(k) process in 2019 (K191373).

Xelma

Xelma consists of amelogenin proteins purified from porcine teeth, propylene glycol alginate (PGA), and water. It has not yet received marketing approval or clearance by the FDA. Amelogenin is a cell adhesion protein, and when suspended in a gelatinous matrix has been proposed to promote cellular growth. The use of Xelma was reported in a single-blind randomized trial involving 123 participants with VSUs (Vowden, 2006). Participants were assigned to receive treatment with either Xelma plus compression therapy (n=62) compared to a mixture of PGA and water plus compression therapy (n=61) and were followed for 12 weeks. The authors of this study state that Xelma outperformed the control group in multiple factors, including percentage of wound size reduction. However, no statistical analysis is presented to support these claims. No data on complication rates was provided.

XenMatrix Surgical Graft

XenMatrix (C.R. Bard, Warwick, RI) is an acellular, sterile, non-pyrogenic, dermal collagen product of bovine origin. XenMatix is intended for implantation to reinforce soft tissue where weakness exists and for surgical repair of damaged or ruptured soft tissue, including: abdominal plastic and reconstructive surgery; muscle flap reinforcement; hernia repair including abdominal, inguinal, femoral, diaphragmatic, scrotal, umbilical, and incisional hernias. The product is cleared through the FDA's 510(k) process (K140501).

Ilahi (2023) reported the results of a prospective case series study involving 75 participants undergoing ventral/incisional midline hernia repair using XenMatrix. The authors reported on surgical site occurrence in the first 45 days post-implantation and length of stay, return to work, hernia recurrence, reoperation, quality of life, and surgical site occurrence at 1, 3, 6, 12, 18, and 24 months. A total of 16 participants (21%) did not complete the study, resulting in complete data for 59 participants (79%). Overall, hernia recurrence was reported to be 5.8%. Device-related adverse events occurred in 4.0% of cases, and reoperation in 10.7%. Only one case of mesh infection was reported (1.3%) and no graft removal was needed. Surgical site occurrence requiring intervention within 45 days post-implantation was reported in 14.7% of participants, and 20.0% > 45 days post-implantation. Surgical complications were evaluated according to the Clavien–Dindo system, with very few grade IVa, IVb, and V hernia-related complications (3%). Complications judged to be grade IIIa or IIIb occurred 37% of participants. The most common hernia-related complications seroma (n=14), bowel obstruction (n=9), pain (n=8), Ileus (n =4), incisional cellulitis (n=4), and surgical site infections (n=4). This study is impaired by several factors, including low power, lack of blinding and comparison groups, and others. Further, the significant loss of complete data makes these results difficult to interpret.

Other studies involving the use of XenMatrix are discussed elsewhere in this document for abdominal wall defect repair (Huntington, 2016; Rosen 2013). Those results are not generalizable to a wider population.

Background/Overview

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Regulatory Processes for Grafting Materials

Soft tissue grafting materials find their way to U.S. market through several regulatory pathways. Oversight for all these pathways is provided by the U.S Food and Drug Administration (FDA).

The Premarket Approval (PMA) Process is detailed in the Code of Federal Regulations Title 21 Part 860. Devices required to undergo this process are those deemed to present the most risk of harm to the public. The PMA process involves several steps of pre-clinical and clinical trials (Phase 0 through III). Each step is reviewed by the FDA to evaluate safety and efficacy data. If the FDA finds the data presented acceptable, a larger and more robust study is authorized until Phase III trials have been completed. Devices which pass Phase III are deemed "Approved" by the FDA and may be marketed in the U.S. This path was used in only a small minority of products addressed in this document. More information regarding the PMA process can be found at: https://www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma.

The "510K" process, also referred to as the Premarket Notification (PMN) process, is named after Section 510(k) of the Food, Drug and Cosmetic Act. This section of the Act requires manufacturers of devices that qualify to notify the FDA of their intent to market a medical device at least 90 days in advance. This law applies to any device that: (1) is not required to undergo review under another pathway, (2) was not already in commercial distribution prior to May 28, 1976, and (3) is to be introduced into commercial distribution for the first time or reintroduced in a significantly changed or modified form that alters its safety or effectiveness. The regulations stipulate that devices applying for 510(k) clearance must demonstrate that they are substantially equivalent to a device with prior PMA approval or marketed prior to May 28, 1976. No significant new data addressing safety or efficacy is required g this process. Devices with this type of review may or may not have undergone rigorous clinical testing to establish the presence or absence of these attributes. Devices passing through this pathway are referred to as "cleared." More information regarding the 510(k) process can be found at: https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k.

A Humanitarian Device Exemption (HDE) is a regulatory path similar to a PMA but is exempt from the effectiveness requirements of sections 514 and 515 of the Code of Federal Regulations Title 21 Part 860, which details the PMA process. A device approved under an HDE is referred to as Humanitarian Use Device (HUD). An HUD is defined as a "medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year." The HDE process is intended to facilitate the development of devices that could benefit individuals with rare conditions for whom medical devices are unlikely to be developed through the PMA process. Devices covered under this regulation are exempt from many of the PMA requirements, but have certain restrictions placed on their use outside the investigational setting. More information regarding the HDE process can be found at: https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/hde-approvals.

There is a specific pathway available for biological tissue derived from human sources deemed as "minimally manipulated." The FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P) is addressed in the Code of Federal Regulations Title 21, volume 8, Part 1271 "Human Cells, Tissues, And Cellular and Tissue-Based Products." These regulations detail the use of human autologous and allographic tissues for transplantation. They specify that "minimally manipulated" tissues undergo proper safeguards to prevent infection or other safety hazards. It should be made clear that products that reach the market through the HCT/P process do NOT require any testing to prove clinical safety or efficacy. Thus, their performance when used in the treatment of

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human participants may or may not have been tested in clinical trials. Human-derived tissues that are deemed to have been more than minimally manipulated are required to undergo one of the other regulatory pathways described above. HCT/Ps are regulated under 21 CFR 1271.3(d)(1) and Section 361 of the PHS Act, which can be found at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=1271.

In the vast majority of cases, soft tissue grafting products are considered devices by the FDA. However, in some rare cases, based upon the composition, preparation, and method of delivery, some products may be considered drugs and reviewed under the FDA's drug regulatory process. Only one product addressed in this document has been so treated and is designated an Orphan Drug. This designation for drugs is similar to the HDE designation for devices. The Code of Federal Regulations Title 21, Part 316 details the "Orphan Drug" process and defines an Orphan Drug as a drug intended for use in a rare disease or condition as outlined in section 526 of the Act. As with HDEs, the Orphan Drug designation is intended to facilitate the development of drugs that could benefit individuals with rare conditions for whom drugs are unlikely to be developed through other regulatory processes. More information regarding the Orphan Drug designation can be found at: http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm.

Skin Wound Care

The skin is the largest organ of the body. It is composed of two layers, the epidermis, and the dermis, and provides functions critical to survival. The skin acts as a protective barrier to fluid losses and dehydration and it protects against infection and injury by providing a barrier to repel bacteria and other organisms. The skin provides sensory contact with our environment that tells us whether we are feeling light touch, pressure, pain, heat, or cold. Damage to the skin that is extensive or prolonged may interfere with these functions or with those of other body systems and may become life-threatening in some circumstances.

The treatment of burns and other wounds that have failed to heal despite conservative measures, referred to as chronic wounds, creates a significant burden on the population in terms of pain, disability, and decreased quality of life. Chronic wounds may be due to the effects of diabetes, venous insufficiency to the extremities, pressure due to prolonged periods in the same body position, and other types of skin injuries. They can be difficult to treat and may require treatment with various coverings, such as skin grafts or other materials to prevent infection, maintain an environment conducive to healing, or provide a medium for re-growth of new skin. Such coverings come in a wide array of types including synthetic materials, tissues from the individuals themselves (autologous), human donors (allogeneic), or from animals such as cows and pigs (xenographic), or any combination of these materials (composites).

The American Diabetes Association (ADA) published Standards of Medical Care in Diabetes in 2025 included the following recommendation regarding DFUs:

12.32 For chronic diabetic foot ulcers that have failed to heal with optimal standard care alone, adjunctive treatment with randomized controlled trial–proven advanced agents should be considered. Considerations might include negative-pressure wound therapy, placental membranes, bioengineered skin substitutes, several acellular matrices, autologous fibrin and leukocyte platelet patches, and topical oxygen therapy.

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Level of evidence A: Defined as Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including:
• Evidence from a well-conducted multicenter trial
• Evidence from a meta-analysis that incorporated quality ratings in the analysis

Surgical Reinforcement Procedures

In a wide variety of surgical procedures, there may be a need for additional reinforcement of soft tissues to strengthen the structures being repaired, such as in abdominal wall repair or orthopedic reconstruction procedures. Traditionally this task is undertaken with the use of allogeneic cadaver-derived grafts or synthetic materials such as polypropylene and Gore-Tex®. However, in some cases such materials may not be appropriate, and other materials have been sought.

In other circumstances, the use of grafting materials has been suggested as a substitute for surgery.

Product types:

Allogeneic Products

There are currently several different types of allogeneic (human-derived) wound care products available. One type involves the use of donated human cadaver skin which is then treated with various methods to remove the cellular material and deactivate or kill pathogens (e.g., AlloDerm, GraftJacket, and Neoform Dermis). This process leaves only the collagen protein scaffold, which has been proposed as an acceptable medium for which new skin cells from the individual can populate and grow into when placed over a wound site.

Another type of allogeneic product includes composite products that may contain human skin cells, keratinocytes and/or fibroblasts (depending upon the product), which are imbedded into a decellularized collagen protein scaffold derived from a xenographic source (e.g., Apligraf, OrCel). Some of these products may also consist of layers of synthetic materials like silicone, nylon, or polyglactin (e.g., Dermagraft).

Autologous Products:

A product derived from the individual's own body or body products

Bioengineered autologous skin-derived products

Bioengineered autologous skin-derived products (for example, MyOwn Skin, SkinTE) involve the harvesting of skin from an individual, which is then processed in a lab where it is altered in a manner that has been proposed to enhance it as a healing vector for wounds.

In a 2022 Cochrane review, Thompson compared licensed bioengineered nerve conduits or nerve wraps used in surgical repair of traumatic peripheral nerve injuries of the upper extremity, to the current gold standard surgical technique (microsurgical repair with use of nerve autografts). The authors concluded that the evidence does not support the use of nerve repair devices over standard repair. There was significant heterogeneity in study methodologies, participants, injury pattern, repair timing, and outcome measures across the studies of the

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bioengineered devices, this made comparisons unreliable. The studies were also small and at risk of bias which made the overall certainty of evidence low or very low. The data provided some evidence that more people may experience adverse events with the use of bioengineered devices than with standard repair and may also be at increased need for revision surgery. There was no data for a primary outcome measure (muscle strength) at 24 months and sensory recovery was uncertain. Additional trials with improved methodologies and a minimum of 12 months' follow-up are needed to analyze the safety and clinical efficacy of bioengineered nerve repair devices.

Composite Products

Composite products are created from a variety of materials of combined origins. Such products usually combine an allogeneic or xenographic collagen-based product with a synthetic one (for example, Avaulta Plus, Integra Matrix, and Integra Bilayer Matrix). Additionally, the development of advanced in vitro culturing techniques has allowed the development of new products which combine human dermal cellular materials with those derived from animals (e.g., Epicel). These products involve the harvesting of human epidermal cells (either from the individual being treated or from donor tissue) which are then cultured with animal cells to produce sheets of biosynthetic skin which have been proposed for use in treating human skin conditions.

Plant Based

A product derived from plant sources (for example VersaWrap).

Synthetic Products

Synthetic treatments include various forms of skin-like coverings, barriers, and devices to augment cartilage and other connective tissues. This category includes wound dressings, silicone/nylon membranes and material to augment or replace cartilage, tendons, and ligaments.

Completely synthetic wound dressings and other grafting products (e.g., Biobrane) are composed of manufactured materials to form a covering for wounds. This type of product may consist of a wide array of materials including silicone, nylon, polypropylene, and polyester.

Xenographic and Xenographic-Related or Derived Products
Many wound care and reconstructive products are made from materials derived from various animal sources including cow, horse, and pig tissues. Most of these products are created by harvesting living tissues (e.g., skin, intestines, tendons, etc.) from a donor animal, which are then processed to remove the cellular content and leave only the collagen protein scaffold. As with such allogeneic products, this scaffold is intended to function as a welcoming environment into which new autologous cells (e.g., skin, tendon, and cartilage) may grow. Most xenographic products are composed of the decellularized collagen scaffold alone (e.g., Collamend, Cuffpatch, Mediskin, Oasis, OrthoADAPT, Pelvicol, Pelvisoft, PriMatrix, Surgisis, Unite).

Xenographic materials have been proposed for many applications including reconstruction procedures of the breast, pelvic floor, abdominal wall, tendons, and others. These products are sewn onto the soft tissues where they are needed to provide support and strengthen the underlying structures. This occurs by the xenograft acting as a bed for new growth of autologous tissue.

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Another type of product is a substance made by or derived from xenographic sources. One such product is honey, which has been proposed as a topical treatment for a wide variety of skin conditions.

Definitions

Diabetic foot ulcer (DFU): A potential complication of diabetes due to prolonged elevated blood sugar levels which can damage blood vessels and nerves throughout the body. A DFU is a slow healing full-thickness wound, through the dermis, below the ankle on a weight-bearing or exposed surface in an individual with diabetes. DFUs are categorized as being neuropathic, ischemic, or neuroischemic (mixed). The most common sites are the plantar surface of the foot and the toes. DFUs are caused by repetitive injury to an insensate or vascularly compromised foot and may lead to amputation.

Equine-derived decellularized collagen products (e.g., OrthADAPT and Unite): This is a type of product derived from purified tissues which are derived from horses. It has been proposed that this type of technology may be used for the repair and reinforcement of soft tissues such as tendons and ligaments, as well as the treatment of skin wounds.

Fresh, frozen, unprocessed allogeneic skin products as those that have undergone procedures necessary for storage and use, like freezing, cryopreservation, and removal of the epidermal layer and hair, without altering their native cell structures (excludes freeze-drying). Any proprietary processes involving anti-infectives, radiation, or heat that could impact the graft's integrity or performance would disqualify a product from being classified as unprocessed.

Hernia meshes of non-biologic origin: These products are either synthetic or biosynthetic:

Biosynthetic: Mesh products are made from resorbable synthetically derived meshes with resorption profiles between 6 and 36 months. Theoretically, this allows native collagen deposition for wound strength and durability while reducing the risks of chronic mesh infection affiliated with permanent synthetic alternatives.

Synthetic: Mesh products are made from either woven extruded monofilament (for example, polypropylene or polyester) or created from expanded polytetrafluoroethylene. They may be subcategorized by; weight/density, material, composition, pore characteristics, and mechanical parameters. Products in this category are permanent and are not absorbed by the body.

Nerve conduits: A bioengineered product used in the repair of traumatic peripheral nerve injuries. The product is used in the reconstruction of a gap defect by placing proximal and distal nerve stumps into a tubular construct. Conduits are intended to replace the need for nerve autograft harvest.
Nerve wraps: A bioengineered sheet of material used in the repair of traumatic peripheral nerve injuries. The product is formed into a tube around approximated nerve stumps, it's purpose is to minimize fibrosis and scarring, and provide a narrow gap to facilitate bridging across the repair site.

Vancouver scar scale: An objective and validated method for describing burn scars that includes a summation of scar characteristics including pigmentation [0-2], vascularity [0-3], pliability [0-5], and height [0-3], normal skin is given a score of 0 for each category.

WHCRA: The Women's Health and Cancer Rights Act of 1998 (WHCRA) is federal legislation that provides that any individual, with insurance coverage who is receiving benefits in connection with a mastectomy covered by their

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benefit plan (whether or not for cancer) who elects breast reconstruction, must receive coverage for the reconstructive services as provided by WHCRA. This includes reconstruction of the breast on which the mastectomy has been performed, surgery and reconstruction of the other breast to produce a symmetrical appearance and prostheses and treatment of physical complications of all stages of the mastectomy including lymphedemas. If additional surgery is required for either breast for treatment of physical complications of the implant or reconstruction, surgery on the other breast to produce a symmetrical appearance is reconstructive at that point as well. The name of this law is misleading because: 1) cancer does not have to be the reason for the mastectomy; and 2) the mandate applies to men, as well as women. WHCRA does not address lumpectomies. Some states have enacted similar legislation, and some states include mandated benefits for reconstructive services after lumpectomy.

Wound infection: A wound with at least some clinical signs and symptoms of infections such as increased exudates, odor, redness, swelling, heat, pain, tenderness to touch, and purulent discharge; quantitative culture is not required.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When Services are Investigational and Not Medically Necessary:

CPT

31574	Laryngoscopy, flexible; with injection(s) for augmentation (eg, percutaneous, transoral), unilateral [when specified as using a skin/tissue substitute such as Cymetra]
46707	Repair of anorectal fistula with plug (eg, porcine small intestine submucosa [SIS])
0627T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with fluoroscopic guidance, lumbar; first level [VAST, Via Disc]
0628T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with fluoroscopic guidance, lumbar; each additional level [VAST, Via Disc]
0629T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with CT guidance, lumbar; first level [VAST, Via Disc]
0630T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with CT guidance, lumbar; each additional level [VAST, Via Disc]

ICD-10 Diagnosis

All diagnoses

Application of skin substitutes and soft tissue grafts:

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When services are Investigational and Not Medically Necessary for application of products listed below:

CPT	
15150	Tissue cultured skin autograft, trunk, arms, legs; first 25 sq cm or less
15151	Tissue cultured skin autograft, trunk, arms, legs; additional 1 sq cm to 75 sq cm
15152	Tissue cultured skin autograft, trunk, arms, legs; each additional 100 sq cm, or each additional 1% of body area of infants and children, or part thereof
15155	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; first 25 sq cm or less
15156	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; additional 1 sq cm to 75 sq cm
15157	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; each additional 100 sq cm, or each additional 1% of body area of infants and children, or part thereof
15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15272	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15274	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15276	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15278	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof
15777	Implantation of biologic implant (eg, acellular dermal matrix) for soft tissue reinforcement (ie, breast, trunk)
17999	Unlisted procedure, skin, mucous membrane and subcutaneous tissue [when specified as implantation of biologic implants for soft tissue reinforcement in tissues other than breast and trunk]
29999	Unlisted procedure, arthroscopy [when specified as a tendon repair using BioBrace implant]

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HCPCS

C5271	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5272	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof
C5273	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5274	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof
C5275	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5276	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof
C5277	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5278	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof

ICD-10 Diagnosis

All diagnoses

Products

When Services are Investigational and Not Medically Necessary:

HCPCS

A2001	Innovamatrix AC, per square centimeter
A2002	Mirragen advanced wound matrix, per square centimeter
A2004	Xcellistem, 1mg
A2005	Microlyte matrix, per square centimeter
A2006	Novosorb synpath dermal matrix, per square centimeter
A2007	Restrata, per square centimeter
A2008	TheraGenesis, per square centimeter
A2009	Symphony, per square centimeter
A2010	Apis, per square centimeter
A2011	Supra SDRM, per square centimeter

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A2012	Suprathel, per square centimeter
A2013	InnovaMatrix FS, per square centimeter
A2014	Omeza Collagen Matrix, per 100 mg
A2015	Phoenix Wound Matrix, per sq cm
A2016	PermeaDerm B, per sq cm
A2017	PermeaDerm Glove, each
A2018	PermeaDerm C, per sq cm
A2019	Kerecis omega3 MariGen Shield, per square centimeter
A2020	Ac5 advanced wound system (Ac5)
A2021	NeoMatriX, per square centimeter
A2022	InnovaBurn or InnovaMatrix XL, per square centimeter
A2023	InnovaMatrix PD 1 mg
A2024	Resolve Matrix or xenoPATCH, per square centimeter
A2025	Miro3D, per cubic centimeter
A2026	Restrata MiniMatrix, 5 mg
A2027	Matriderm, per square centimeter
A2028	MicroMatrix Flex, per mg
A2029	MiroTract Wound Matrix sheet, per cubic centimeter
A2030	Miro3D fibers, per milligram
A2031	MiroDry wound matrix, per square centimeter
A2032	Myriad matrix, per square centimeter
A2033	Myriad morcells, 4 milligrams
A2034	Foundation DRS Solo, per sq cm
A2035	Corplex P or Theracor P or Allacor P, per milligram
A4100	Skin substitute, FDA-cleared as a device, not otherwise specified [when describing a product with no specific code indicated as investigational and not medically necessary]
C1763	Connective tissue, non-human (includes synthetic) [when specified as BioBrace Implant]
C9352	Microporous collagen implantable tube (NeuraGen Nerve Guide), per centimeter length
C9353	Microporous collagen implantable slit tube (NeuraWrap Nerve Protector), per centimeter length
C9354	Acellular pericardial tissue matrix of non-human origin (Veritas), per square centimeter
C9355	Collagen nerve cuff (NeuroMatrix), per 0.5 centimeter length
C9356	Tendon, porous matrix of cross-linked collagen and glycosaminoglycan matrix (TenoGlide Tendon Protector Sheet), per square centimeter
C9361	Collagen matrix nerve wrap (NeuroMend Collagen Nerve Wrap), per 0.5 centimeter length
C9364	Porcine implant, Permacol, per square centimeter
C9399	Unclassified drugs or biologicals [when describing a product with no specific code indicated as investigational and not medically necessary]
C9796	Repair of enterocutaneous fistula small intestine or colon (excluding anorectal fistula) with plug (e.g., porcine small intestine submucosa [sis])
G0428	Collagen meniscus implant procedure for filling meniscal defects (e.g., CMI, collagen scaffold, Menaflex)
Q4100	Skin substitute, not otherwise specified [when describing a product with no specific code indicated as investigational and not medically necessary]

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Q4103	Oasis Burn Matrix, per square centimeter
Q4108	Integra Matrix, per square centimeter
Q4111	Gammagraft, per square centimeter
Q4112	Cymetra, injectable, 1 cc
Q4113	Graftjacket Xpress, injectable, 1 cc
Q4114	Integra Flowable Wound Matrix, injectable, 1 cc
Q4117	Hyalomatrix, per square centimeter
Q4118	Matristem micromatrix, 1 mg
Q4123	AlloSkin RT, per square centimeter
Q4125	ArthroFlex, per square centimeter
Q4126	Memoderm, dermaspan, tranzgraft or integuply, per square centimeter
Q4127	Talymed, per square centimeter
Q4132	Grafix CORE and GrafixPL CORE, per square centimeter
Q4134	hMatrix, per square centimeter
Q4135	Mediskin, per square centimeter
Q4137	AmnioExCel, AmnioExCel plus or BioDExCel, per square centimeter
Q4138	BioDfence Dryflex, per square centimeter
Q4139	AmnioMatrix or BioDMatrix, injectable, 1 cc
Q4140	BioDfence, per square centimeter
Q4141	Alloskin AC, per square centimeter
Q4142	XCM Biologic Tissue Matrix, per square centimeter
Q4143	Repriza, per square centimeter
Q4145	Epifix, injectable, 1 mg
Q4146	TenSIX, per square centimeter
Q4147	Architect, Architect PX, or Architect FX, extracellular matrix, per square centimeter
Q4148	NEOX Cord 1k, NEOX Cord RT, or Clarix Cord 1k, per square centimeter
Q4149	Excellagen, 0.1 cc
Q4150	Allowrap DS or Dry, per square centimeter
Q4152	DermaPure, per square centimeter
Q4153	Dermavest and Plurivest, per square centimeter
Q4155	NeoxFlo or ClarixFlo, 1 mg
Q4156	NEOX 100 or Clarix 100, per square centimeter
Q4157	Revitalon, per square centimeter
Q4159	Affinity, per square centimeter
Q4161	Bio-connekt wound matrix, per square centimeter
Q4162	WoundEx Flow, BioSkin Flow, 0.5 cc
Q4163	WoundEx, BioSkin, per square centimeter
Q4164	Helicoll, per square centimeter
Q4165	Keramatrix or Kerasorb, per square centimeter
Q4166	Cytal, per square centimeter [formerly Matristem wound/burn matrix]
Q4167	TruSkin, per square centimeter
Q4169	Artacent Wound, per square centimeter
Q4170	CYGNUS, per square centimeter
Q4171	Interfyl, 1 mg
Q4173	PalinGen or PalinGen Xplus, per square centimeter

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Q4174	PalinGen or ProMatrX, 0.36 mg per 0.25 cc
Q4175	Miroderm, per square centimeter
Q4176	NeoPatch or Therion, per square centimeter
Q4177	FlowerAmnioflo, 0.1 cc
Q4178	FlowerAmniopatch, per square centimeter
Q4179	FlowerDerm, per square centimeter
Q4180	Revita, per square centimeter
Q4181	Amnio Wound, per square centimeter
Q4183	Surgigraft, per square centimeter
Q4184	Cellesta or Cellesta Duo, per square centimeter
Q4185	Cellesta flowable amnion (25 mg per cc); per 0.5 cc
Q4188	Amnioarmor, per square centimeter
Q4189	Artacent AC, 1 mg
Q4190	Artacent AC, per square centimeter
Q4191	Restorigin, per square centimeter
Q4192	Restorigin, 1 cc
Q4193	Coll-e-derm, per square centimeter
Q4194	Novachor, per square centimeter
Q4195	Puraply, per square centimeter
Q4196	PuraPly AM, per square centimeter
Q4197	PuraPly XT, per square centimeter
Q4198	Genesis amniotic membrane, per square centimeter
Q4199	Cygnus matrix, per square centimeter
Q4200	Skin TE, per square centimeter
Q4201	Matrion, per square centimeter
Q4202	Keroxx (2.5g/cc), 1cc
Q4203	Derma-gide, per square centimeter
Q4204	Xwrap, per square centimeter
Q4205	Membrane graft or Membrane wrap, per square centimeter
Q4206	Fluid flow or Fluid GF, 1 cc
Q4208	Novafix, per square centimeter
Q4209	SurGraft, per square centimeter
Q4211	Amnion bio or AxoBioMembrane, per square centimeter
Q4212	AlloGen, per cc
Q4213	Ascent, 0.5 mg
Q4214	Cellesta cord, per square centimeter
Q4215	Axolotl Ambient or Axolotl Cryo, 0.1 mg
Q4216	Artacent cord, per square centimeter
Q4217	Woundfix, BioWound, Woundfix Plus, BioWound Plus, Woundfix Xplus or BioWound Xplus, per square centimeter
Q4218	Surgicord, per square centimeter
Q4219	SurgiGRAFT-Dual, per square centimeter
Q4220	BellaCell HD or Surederm, per square centimeter
Q4221	Amniowrap2, per square centimeter
Q4222	Progenamatrix, per square centimeter

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Q4224	Human health factor 10 amniotic patch (hhf10-p), per square centimeter
Q4225	Amniobind or DermaBind TL, per square centimeter
Q4226	MyOwn Skin, includes harvesting and preparation procedures, per square centimeter
Q4227	AmnioCore, per square centimeter
Q4229	Cogenex amniotic membrane, per square centimeter
Q4230	Cogenex flowable amnion, per 0.5 cc
Q4232	Corplex, per square centimeter
Q4233	SurFactor or NuDyn, per 0.5 cc
Q4234	Xcellerate, per square centimeter
Q4235	Amniorepair or AltiPly, per square centimeter
Q4236	CarePATCH, per square centimeter
Q4237	Cryo-cord, per square centimeter
Q4238	Derm-Maxx, per square centimeter
Q4239	Amnio-Maxx or Amnio-Maxx Lite, per square centimeter
Q4240	CoreCyte, for topical use only, per 0.5 cc
Q4241	PolyCyte, for topical use only, per 0.5 cc
Q4242	AmnioCyte Plus, per 0.5 cc
Q4245	Amniotext, per cc
Q4246	Coretext or Protext, per cc
Q4247	Amniotext patch, per square centimeter
Q4248	Dermacyte Amniotic Membrane Allograft, per square centimeter
Q4249	Amniply, for topical use only, per square centimeter
Q4250	AmnioAMP-MP, per square centimeter
Q4251	Vim, per sq cm
Q4252	Vendaje, per sq cm
Q4253	Zenith Amniotic Membrane, per sq cm
Q4254	Novafix DL, per square centimeter
Q4255	REGUaRD, for topical use only, per square centimeter
Q4256	MLG-complete, per square centimeter
Q4257	Relese, per square centimeter
Q4258	Enverse, per square centimeter
Q4259	Celera dual layer or celera dual membrane, per square centimeter
Q4260	Signature Apatch, per square centimeter
Q4261	TAG, per square centimeter
Q4262	Dual Layer Impax Membrane, per square centimeter
Q4263	SurGraft TL, per square centimeter
Q4264	Cocoon membrane, per square centimeter
Q4265	NeoStim TL, per square centimeter
Q4266	NeoStim membrane, per square centimeter
Q4267	NeoStim DL, per square centimeter
Q4268	SurGraft FT, per square centimeter
Q4269	SurGraft XT, per square centimeter
Q4270	Complete SL, per square centimeter
Q4271	Complete FT, per square centimeter
Q4272	Esano A, per square centimeter

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Q4273	Esano AAA, per square centimeter
Q4274	Esano AC, per square centimeter
Q4275	Esano ACA, per square centimeter
Q4276	Orion, per square centimeter
Q4278	EPIEFFECT, per square centimeter
Q4279	Vendaje AC, per square centimeter
Q4280	Xcell amnio matrix, per square centimeter
Q4281	Barrera SL or Barrera DL, per square centimeter
Q4282	Cygnus Dual, per square centimeter
Q4284	DermaBind SL, per square centimeter
Q4285	NuDYN DL or NuDYN DL mesh, per square centimeter
Q4286	NuDYN SL or NuDYN SLW, per square centimeter
Q4287	DermaBind DL, per square centimeter
Q4288	DermaBind CH, per square centimeter
Q4289	RevoShield + Amniotic Barrier, per square centimeter
Q4290	Membrane Wrap-Hydro, per square centimeter
Q4291	Lamellas XT, per square centimeter
Q4292	Lamellas, per square centimeter
Q4293	Acesso DL, per square centimeter
Q4294	Amnio Quad-Core, per square centimeter
Q4295	Amnio Tri-Core amniotic, per square centimeter
Q4296	Rebound Matrix, per square centimeter
Q4297	Emerge Matrix, per square centimeter
Q4298	AmnioCore Pro, per square centimeter
Q4299	AmniCore Pro+, per square centimeter
Q4300	Acesso TL, per square centimeter
Q4301	Activate Matrix, per square centimeter
Q4302	Complete ACA, per square centimeter
Q4303	Complete AA, per square centimeter
Q4304	Grafix Plus, per square centimeter
Q4305	American amnion AC tri-layer, per square centimeter
Q4306	American amnion AC, per square centimeter
Q4307	American amnion, per square centimeter
Q4308	Sanopellis, per square centimeter
Q4309	VIA Matrix, per square centimeter
Q4310	Procenta, per 100 mg
Q4311	Acesso, per square centimeter
Q4312	Acesso AC, per square centimeter
Q4313	DermaBind FM, per square centimeter
Q4314	Reeva FT, per square centimeter
Q4315	RegeneLink Amniotic Membrane allograft, per square centimeter
Q4316	AmchoPlast, per square centimeter
Q4317	VitoGraft, per square centimeter
Q4318	E-Graft, per square centimeter
Q4319	SanoGraft, per square centimeter

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Q4320	PelloGraft, per square centimeter
Q4321	RenoGraft, per square centimeter
Q4322	CaregraFT, per square centimeter
Q4323	alloPLY, per square centimeter
Q4324	AmnioTX, per square centimeter
Q4325	ACApatch, per square centimeter
Q4326	WoundPlus, per square centimeter
Q4327	DuoAmnion, per square centimeter
Q4328	MOST, per square centimeter
Q4329	Singlay, per square centimeter
Q4330	TOTAL, per square centimeter
Q4331	Axolotl Graft, per square centimeter
Q4332	Axolotl DualGraft, per square centimeter
Q4333	ArdeoGraft, per square centimeter
Q4336	Artacent C, per square centimeter
Q4337	Artacent Trident, per square centimeter
Q4338	Artacent Velos, per square centimeter
Q4339	Artacent VeriClen, per square centimeter
Q4340	SimpliGraft, per square centimeter
Q4341	SimpliMax, per square centimeter
Q4342	TheraMend, per square centimeter
Q4343	Dermacyte AC matrix amniotic membrane allograft, per square centimeter
Q4344	Tri-membrane wrap, per square centimeter
Q4345	Matrix HD allograft dermis, per square centimeter
Q4346	Shelter DM Matrix, per square centimeter
Q4347	Rampart DL Matrix, per square centimeter
Q4348	Sentry SL Matrix, per square centimeter
Q4349	Mantle DL Matrix, per square centimeter
Q4350	Palisade DM Matrix, per square centimeter
Q4351	Enclose TL Matrix, per square centimeter
Q4352	Overlay SL Matrix, per square centimeter
Q4353	Xceed TL Matrix, per square centimeter
Q4354	PalinGen dual-layer membrane, per square centimeter
Q4355	Abiomend Xplus membrane and abiomend Xplus hydromembrane, per square centimeter
Q4356	Abiomend membrane and abiomend hydromembrane, per square centimeter
Q4357	Xwrap Plus, per square centimeter
Q4358	Xwrap Dual, per square centimeter
Q4359	Choriply, per square centimeter
Q4360	AmchoPlast FD, per square centimeter
Q4361	EpiXpress, per square centimeter
Q4362	Cygnus Disk, per square centimeter
Q4363	Amnio Burgeon Membrane and Hydromembrane, per square centimeter
Q4364	Amnio Burgeon Xplus Membrane and Xplus Hydromembrane, per square centimeter
Q4365	Amnio Burgeon Dual-Layer Membrane, per square centimeter
Q4366	Dual Layer Amnio Burgeon X-Membrane, per square centimeter

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Q4367	AmnioCore SL, per square centimeter

ICD-10 Diagnosis

All diagnoses

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Peer Reviewed Publications:

Non-Product Specific Acellular Dermal Matrix (ADM) Studies, Multiple Product Studies, Meta-analyses, and Systematic Reviews

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3. Haug V, Tapking C, Panayi AC, et al. Outcome comparison of the most commonly employed wound coverage techniques in patients with massive burns ≥50% TBSA - A systematic review and meta-analysis. Burns: journal of the International Society for Burn Injuries. 2024; 50(9):107210.
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5. Ho G, Nguyen TJ, Shahabi A, et al. A systematic review and meta-analysis of complications associated with acellular dermal matrix-assisted breast reconstruction. Ann Plast Surg. 2012; 68(4):346-356.
6. Kim JY, Davila AA, Persing S, et al. A meta-analysis of human acellular dermis and submuscular tissue expander breast reconstruction. Plast Reconstr Surg. 2012; 129(1):28-41.
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11. Silverstein ML, Momeni A. Long-term outcomes following hybrid breast reconstruction. Plast Reconstr Surg. 2024; 154(2):217e-223e. Epub 2023 Aug 11.
12. Sorkin M, Qi J, Kim HM, et al. Acellular dermal matrix in immediate expander/implant breast reconstruction: a multicenter assessment of risks and benefits. Plast Reconstr Surg. 2017; 140(6):1091-1100.
13. van den Bosch AS, Verwilligen RAF, Pijpe A, et al. Outcomes of dermal substitutes in burns and burn scar reconstruction: A systematic review and meta-analysis. Wound Repair Regen. 2024; 32(6):960-978. Epub 2024 Oct 22.
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Allograft (unspecified)

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1. Buchberger B, Follmann M, Freyer D, et al. The evidence for the use of growth factors and active skin substitutes for the treatment of non-infected diabetic foot ulcers (DFU): a health technology assessment (HTA). Exp Clin Endocrinol Diabetes. 2011; 119(8):472-479.
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Ac5

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Affinity

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Allomax

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AlloPatch

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AMNIOEXCEL

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Amniofix

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Clarix

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Xenograft

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Revised	05/08/2025	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Description/Scope. Removed AmnioBand particulate and ReNu injection from INV and NMN list. Added MiroTract® Wound Matrix to INV and NMN list. Revised Rationale, Definitions, References, and Websites sections. Revised Coding section, removed Q4168 no longer addressed.
	04/16/2025	Updated Coding section to add missing descriptor for A2034 and missing NOC A4100. Note that history section below should indicate addition of NOC 29999 instead of 20999.
Revised	02/20/2025	MPTAC review. Revised Title and Scope. Removed content related to MN products and transitioned that content to CG-SURG-127. Added new products to INV and NMN statement. Revised Rationale, References, and Websites sections. Revised Coding section to include 04/01/2025 HCPCS changes, added A2030-A2035, Q4354-Q4367 and removed Q4231 deleted as of 04/01/2025; also added NOC 20999 and HCPCS C1763; removed codes 15011-15018, 65778, 65779, 65780, C1832, C8002, C9358, C9360, C9363, Q4101, Q4102, Q4104, Q4105, Q4106, Q4107, Q4110, Q4115, Q4116, Q4121, Q4122, Q4124, Q4128, Q4130, Q4133, Q4136, Q4151, Q4154, Q4158, Q4160, Q4186, Q4187, Q4283, Q4334, Q4335, V2790 now addressed in CG-SURG-127.
	01/30/2025	Updated Coding section with 01/01/2025 CPT and HCPCS changes, added 15011-15018, C8002, Q4346, Q4347, Q4348, Q4349, Q4350, Q4351, Q4352, Q4353.
	10/01/2024	Updated Coding section with 10/01/2024 HCPCS changes, revised descriptor for A2024 and added A2027, A2028, A2029, Q4334, Q4335, Q4336, Q4337, Q4338, Q4339, Q4340, Q4341, Q4342, Q4343, Q4344, Q4345.
Revised	05/09/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised ocular indications, including addition of SurSight to MN and NMN section and added new MN criterion addressing non-healing or persistent corneal epithelial defects. Removed VersaWrap from INV and NMN statement. Removed Phasix Mesh from INV and NMN statement. Added Phasix Mesh and Phasix ST Mesh to MN and NMN statements. Updated Rationale, References, and Websites sections. Updated Coding section with 07/01/2024 HCPCS changes to add Q4311-Q4333 and remove Q4210, Q4277 deleted as of 07/01/2024; also revised Coding section for ocular indications including removing Q4290, and added Phasix to NOC codes.
	02/15/2024	MPTAC review. Revised MN statement to include Cortiva and SurgiMend for breast reconstruction. Revised MN statement to include EPICEL, Integra Omnigraft Dermal Regeneration Template, and ReCell for the treatment of

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		partial and deep thickness burns. Revised MN statement to include Biovance and Oasis for the treatment of diabetic foot ulcers. Revised NMN statement to align with revisions to MN statements. Added new products to the INV and NMN statement. Updated Definitions, Background, Discussion, References, and Websites sections. Updated Coding section to include 04/01/2024 HCPCS changes, added Q4310 replacing Q4244 deleted as of 04/01/2024, also added A2026, C9796, Q4305, Q4306, Q4307, Q4308, Q4309.
	12/28/2023	Updated Coding section with 01/01/2024 HCPCS changes, added Q4279, Q4287, Q4288, Q4289, Q4290, Q4291, Q4292, Q4293, Q4294, Q4295, Q4296, Q4297, Q4298, Q4299, Q4300, Q4301, Q4302, Q4303, Q4304 and revised descriptor for Q4225.
	09/27/2023	Updated Coding section with 10/01/2023 HCPCS changes to add A2022, A2023, A2024, A2025, Q4285 and Q4286; also added HCPCS code C1832.
	06/28/2023	Updated Coding section with 07/01/2023 HCPCS changes, added Q4272, Q4273, Q4274, Q4275, Q4276, Q4277, Q4278, Q4280, Q4281, Q4282, Q4283, Q4284. Updated URL for HCT/Ps information site.
Revised	02/16/2023	MPTAC review. Revised MN statement to include SimpliDerm for breast reconstruction. Revised MN statement to include Kerecis and TheraSkin for diabetic foot ulcers. Revised MN statement to include AmnioBand for venous stasis ulcers. Revised MN statement to include OviTex for complex abdominal wall wounds. Revised formatting in several MN statements. Revised NMN statement to align with revisions to MN statements. Added new products to the INV and NMN statement. Updated Rationale, Coding and References sections. Updated Coding section with 04/01/2023 HCPCS changes; added A2019, A2020, A2021, Q4265, Q4266, Q4267, Q4268, Q4269, Q4270, Q4271.
	12/28/2022	Updated Coding section with 01/01/2023 HCPCS changes; added Q4262, Q4263, Q4264, and added Q4236 (code reactivated).
	09/28/2022	Updated Coding section with 10/01/2022 HCPCS changes; revised descriptor for Q4128 and added A2014, A2015, A2016, A2017, A2018.
Revised	05/12/2022	MPTAC review. Revised INV and NMN statement for products with MN indications. Updated Rationale and References sections. Updated Coding section, including 07/01/2022 HCPCS changes; added Q4259, Q4260, Q4261 and revised A2004 descriptor.
Revised	02/17/2022	MPTAC review. Moved StrataGraft from INV and NMN section to MN section for burns. Added mVASC to MN section for treatment of DUFs. Clarified product terminology regarding AlloDerm products. Added new products to INV and NMN statement. Updated Rationale and References sections. Updated Coding section to include MN indications for StrataGraft and mVASC (NOC codes) and 04/01/2022 HCPCS updates to add A2011, A2012, A2013, A4100, Q4224, Q4225, Q4256, Q4257, Q4258.
Revised	11/11/2021	MPTAC review. Updated title and scope to include bioengineered products. Reorganized MN section by indication. Simplified criteria for treatment of DFUs and venous stasis ulcers. Incorporated position statement addressing bioengineered autologous skin-derived products from MED.00110. Added new products to INV and NMN statement. Updated Description/Scope, Rationale,

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		Background, and References sections. Updated Coding section with 01/01/2022 HCPCS changes to add A2001-A2002, A2004-A2010 and Q4199 effective 01/01/2022, also added Q4200, Q4226 previously addressed in MED.00110.
	10/01/2021	Updated Coding section with 10/01/2021 HCPCS changes; added Q4251, Q4252, Q4253 effective 10/01/2021 and removed Q4228, Q4236 deleted 09/30/2021.
Revised	11/05/2020	MPTAC review. Added new MN statement for TheraSkin for treatment of lower extremity dermal wounds. Revised note addressing fresh frozen unprocessed allograft skin products. Revised several statements to begin with the name of the product. Revised IVN and NMN statement for products which have MN indications. Added new products to INV and NMN statement. Updated Scope, Rationale, and References sections. Updated Coding section to include 01/01/2021 CPT changes adding 0627T-0630T.
	10/01/2020	Updated Coding section with 10/01/2020 HCPCS changes to add Q4249, Q4250, Q4254, Q4255, and also 10/01/2020 ICD-10-CM changes adding H18.599 replacing H18.59 deleted 09/30/2020.
	07/01/2020	Updated Coding section with 07/01/2020 HCPCS changes to add Q4227-Q4242, Q4244-Q4248 and revised descriptor for Q4176; also removed C1878, L8607 now addressed in MED.00132.
Revised	11/07/2019	MPTAC review. Moved AmbioDisk from INV and NMN statement to the MN statement addressing of allogeneic amniotic membrane-derived grafts or wound coverings. Added Artacent Ocular to MN statement addressing of allogeneic amniotic membrane-derived grafts or wound coverings. Added new products to INV and NMN statement. Updated Rationale and References sections.
	10/01/2019	Updated Coding section with 10/01/2019 HCPCS changes; added Q4205-Q4206, Q4208-Q4222, revised descriptors for Q4122, Q4165, Q4184; also added C1878.
	06/18/2019	Correction to MN statement addressing amniotic membrane-derived products for conjunctival and corneal indications made. Kerasys removed and replaced by AmnioGraft.
Revised	06/06/2019	MPTAC review. Added new MN and INV and NMN statements addressing amniotic membrane-derived products for conjunctival and corneal indications. Added new products to INV and NMN statement. Updated Rationale, Coding and References sections.
Revised	01/24/2019	MPTAC review. Added new MN statements for EpiCord, Grafix PRIME, and the sheet or membrane form of AmnioBand. Revised INV and NMN statements regarding those products. Added EpiBurn to INV and NMN statement. Updated Coding, Rationale, and References sections.
	12/27/2018	Updated Coding section with 01/01/2019 HCPCS changes; removed Q4131, Q4172 deleted 12/31/2018.
Revised	09/13/2018	MPTAC review. Added several products to the INV and NMN section. Updated Rationale, Coding and References sections.
Revised	01/25/2018	MPTAC review. Revised criteria for EpiFix and Integra Bilayer Matrix Wound Dressing. Deleted statement regarding TransCyte. Moved several products from the INV and NMN section to the MN section. Updated Rationale and References sections. Updated Coding section to include removing Q4182 no longer addressed.

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	12/27/2017	The document header wording updated from "Current Effective Date" to "Publish Date." Updated Coding section with 01/01/2018 HCPCS changes; added codes Q4176-Q4182, descriptor revisions for Q4132, Q4133, Q4148, Q4156, Q4158, Q4162, Q4163.
Revised	08/03/2017	MPTAC review. Added new products to INV and NMN list. Removed Perlane and Restylane from Inv and NMN list. Updated Rationale, Coding and References sections.
Revised	02/02/2017	MPTAC review. Made minor typographical revisions to Position Statement. Added new products to INV and NMN list. Updated Rationale and References sections.
	01/01/2017	Updated Coding section with 01/01/2017 CPT and HCPCS changes; removed codes C9349, Q4119, Q4120, Q4129 deleted 12/31/2016.
Revised	05/05/2016	MPTAC review. Added AlloDerm Ready to Use as MN for the same indications as AlloDerm Regenerative Tissue Matrix. Added FlexHD as MN for breast reconstruction surgery. Clarified INV and NMN statement regarding fresh frozen allograft products. Added new products to the INV and NMN list. Updated Rationale, Coding, and References sections.
Revised	11/05/2015	MPTAC review. Added Restlyane and Perlane to investigational and not medically necessary list. Updated Rationale and References sections. Updated Coding section with 01/01/2016 HCPCS changes; also removed ICD-9 codes.
	07/01/2015	Updated Coding section with 07/01/2015 HCPCS change to descriptor for C9349.
Revised	05/07/2015	MPTAC review. Added new medically necessary position statement regarding the use of fresh, frozen, unprocessed skin allograft products for the treatment of full-thickness or deep partial-thickness burns when criteria are met. Added new products to investigational and not medically necessary section. Updated Rationale, Coding, and References sections.
Revised	02/05/2015	MPTAC review. Added new medically necessary position statement regarding the use the sheet or membrane form of EpiFix. Revised investigational and not medically necessary statement to differentiate between the sheet or membrane form of EpiFix and the particulate or injectable form of EpiFix. Added new products to investigational and not medically necessary section. Updated Rationale, Background, Coding, and References sections. Revised position statements were finalized in a follow-up vote on 03/04/2015.
	01/01/2015	Updated Coding section with 01/01/2015 HCPCS changes.
Revised	02/13/2014	MPTAC review. Clarified nomenclature of AlloDerm product in medically necessary section. Added new products to investigational and not medically necessary section. Updated Rationale, Background, and References sections.
	01/01/2014	Updated Coding section with 01/01/2014 CPT and HCPCS changes.
Revised	08/08/2013	MPTAC review. Added new products to Investigational and Not Medically Necessary list. Updated Rationale and References sections.
Revised	05/09/2013	MPTAC review. Added new products to Investigational and Not Medically Necessary list. Updated Rationale, Coding, and Reference sections.
	01/01/2013	Updated Coding section with 01/01/2013 HCPCS changes; removed C9366, C9368, C9369 deleted 12/31/2012.

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Revised	05/10/2012	MPTAC review. Deleted "autologous" from title. Split off growth factors, silver-based products and autologous tissues for wound treatment and soft tissue to a new policy (MED.00110). Reorganized position statement section. Clarified Medically necessary statement for Apligraf regarding number of applications and deleted corresponding investigational and not medically necessary statement. Added new products to investigational and not medically necessary position statement. Revised Rationale, Background, References, and Index sections. Updated Coding section to include 07/01/2012 HCPCS changes.
	01/19/2012	Updated Coding section with correct diagnosis coding for Apligraf; removed HCPCS codes G0440, G0441 deleted 12/31/2011.
	01/01/2012	Updated Coding section with 01/01/2012 CPT and HCPCS changes; removed codes 15170, 15171, 15175, 15176, 15330, 15331, 15335, 15336, 15340, 15341, 15360, 15361, 15365, 15366, 15400, 15401, 15420, 15421, 15430, 15431, C9365 deleted 12/31/2011; also removed CPT 15150, 15151, 15152, 15155, 15156, 15157.
Revised	05/19/2011	MPTAC review. Added synthetic soft-tissue grafting materials as investigational and not medically necessary to Section I. Added xenographic-related or derived products as investigational and not medically necessary to Section IV. Updated Rationale, References, and Index sections. Updated Coding section with 07/01/2011 HCPCS changes.
Revised	02/17/2011	MPTAC review. Added use of cryopreserved allogeneic human skin to the Allogeneic section as investigational and not medically necessary. Updated Rationale, Coding, References, and Index sections.
	01/01/2011	Updated Coding section with 01/01/2011 HCPCS changes; removed Q4109 deleted 12/31/2010.
Revised	08/19/2010	MPTAC review. Added use of synthetic fistula plugs to synthetic products section as investigational and not medically necessary. Expanded investigational and not medically necessary statement for Dermagraft to cover all indications not listed as medically necessary. Revised language in xenographic investigational and not medically necessary statement. Updated list of xenographic products, including Menaflex™ Collagen Meniscus Implant. Added new section addressing composite autologous / allogeneic / xenographic products. Updated Rationale, Background, Coding, and References sections.
	07/01/2010	Updated Coding section with 07/01/2010 CPT and HCPCS changes.
	01/01/2010	Updated Coding section with 01/01/2010 CPT changes; removed CPT 0170T deleted 12/31/2009.
Revised	08/27/2009	MPTAC review. Added Platelet Rich Plasma as investigational and not medically necessary. Updated coding and Index sections.
Reviewed	05/21/2009	MPTAC review. Added note stating that this document does not address the use of meshes or patches of non-biologic origin when used for standard hernia repair procedures. Updated Index section. Updated coding section with 07/01/2009 HCPCS changes.
Revised	02/26/2009	MPTAC review. Added Investigational and Not Medically Necessary statements for C-QUR and Strattice.

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Revised	11/20/2008	MPTAC review. Added AlloDerm as medically necessary for breast reconstruction and complex abdominal wall wound closure. Updated Rationale and Reference sections. Updated coding section with 01/01/2009 HCPCS changes; removed C9357, J7340, J7341, J7342, J7343, J7344, J7346, J7347, J7348, J7349 deleted 12/31/2008.
Revised	08/28/2008	MPTAC review. Added Vitagel to Investigational and Not Medically Necessary statement of Section II Autologous Products. Added Cymetra to Investigational and Not Medically Necessary statement of Section III Allogeneic Products. Updated Background. Coding section updated to include 10/01/2008 ICD-9 changes.
Revised	05/15/2008	MPTAC review. Changed title from "Wound Healing: Skin Substitutes and Blood-Derived Growth Factors" to "Autogous, Allogeneic, Xenographic, Synthetic and Composite Products for Wound Healing and Soft Tissue Grafting." Reorganized Position Statement section. Added position statements regarding the following products: Actisorb, Avaulta Plus, Collamend, CuffPatch, Mediskin, Neoform Dermis, Pelcvicol, Pelvisoft, Silversorb, and Unite. Revised Rationale, Coding, Background, Definitions, References, and Index sections. Deleted information regarding Procuren®. Updated Coding section with 07/01/2008 HCPCS changes.
Revised	02/21/2008	MPTAC review. Added position statements for Integra™ Matrix Wound Dressing, Primatrix, and TissueMend. Expanded investigational and not medically necessary statement for Surgisis, Autogel and Safeblood to include all indications. Updated Rationale, Background, Definitions, and References sections.
	01/01/2008	Updated Coding section with 01/01/2008 HCPCS changes; removed HCPCS C9351, J7345 deleted 12/31/2007. The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary." This change was approved at the November 29, 2007 MPTAC meeting.
Revised	05/17/2007	MPTAC review. Added the use of AlloDerm for breast reconstruction or augmentation to investigational/not medically necessary statement. Updated Rationale and References sections.
	01/01/2007	Updated Coding section with 01/01/2007 CPT/HCPCS changes.
Revised	09/14/2006	MPTAC review. Added position statement for Surgisis®; updated rationale, background and reference sections. Coding updated; removed CPT 15342, 15343 deleted 12/31/05, HCPCS Q0182, Q0183 deleted 12/31/04.
Revised	03/23/2006	MPTAC review. Added position statement for AlloDerm® and GraftJacket™.
	01/01/2006	Updated Coding section with 01/01/2006 CPT/HCPCS changes
	11/22/2005	Added reference for Centers for Medicare and Medicaid Services (CMS) – National Coverage Determination (NCD).
Revised	07/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger Wellpoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title

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Anthem, Inc.	04/28/2005	SURG.00011	Wound Healing: Tissue Engineered Skin Substitutes and Growth Factors
WellPoint Health Networks, Inc.	04/28/2005	3.02.03	Human Skin Equivalent Grafts
	09/23/2004	8.01.08	Autologous Blood Derived Preparations for Wound Healing

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