The effects of cross-linking in biologic grafts

Natural vs. chemical cross-linking

All biologic grafts are naturally cross-linked, but some are also chemically cross-linked during processing.

Natural cross-linking, a common biological reaction joining two or more molecules by a covalent bond, occurs in the mammalian body as connective tissue forms, catalyzed by native enzymes. This normal process provides strength and makes biologic grafts formed from these tissues—such as Biodesign—effective in soft-tissue repair without additional chemical cross-linking, a process used during the manufacture of some other grafts on the market.

The chemical cross-linking process, sometimes called tanning, mimics natural cross-linking by treating biologic grafts with harsh chemicals, making them resistant to degradation in vivo. However, controlled degradation of the graft is an important step in healing because it signals the surrounding tissue to repair the wound. When degradation is inhibited, cellular attraction is inhibited.[1] Additionally, chemical cross-linking alters the three-dimensional structure of the graft, inhibiting host cell infiltration.[2-4] See Figure 1 below and notice the degree of cell infiltration in non-cross-linked Biodesign and a cross-linked biologic graft.

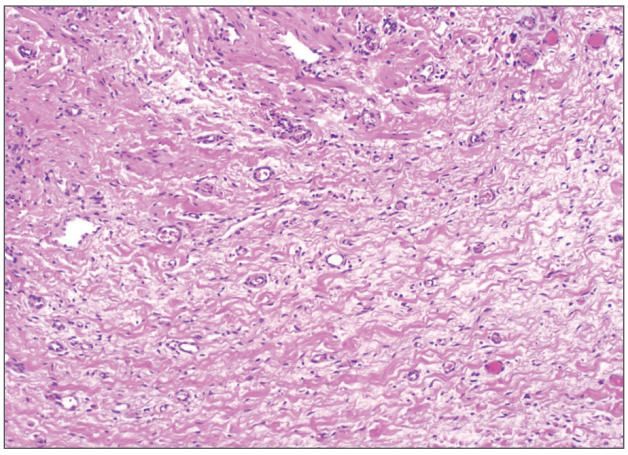
The chemicals used in the tanning process can also release cytotoxic residues,[5] induce calcification of the graft,[6] and cause the body to react as if the graft is foreign,[2] provoking inflammation and encapsulation.[7]

Chemically cross-linked grafts

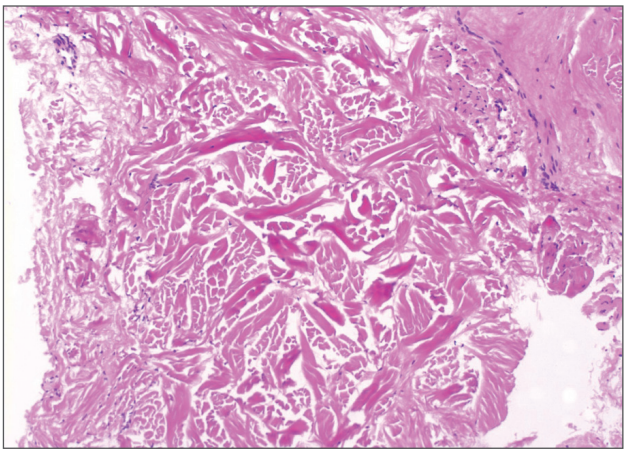
Some biologic grafts on the market are chemically cross-linked during processing. According to one manufacturer of chemically cross-linked grafts, its grafts are chemically cross-linked for "long-lasting dimensional stability."[8] Published results support this outcome but also demonstrate that this can lead to detrimental results.[2] Chemically cross-linked biologic grafts can remain in the body like synthetic mesh—with the associated unwanted results and risks.

(continued on back)

Figure 1: Histologic images showing the extent of cellular infiltration (purple dots) in Biodesign and a cross-linked material.



Biodesign at 8 months



Cross-linked material at 26 months.

(continued from front)

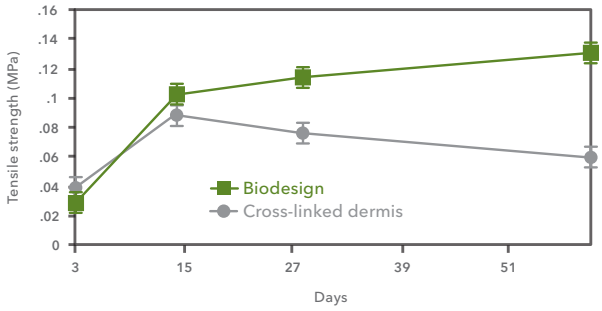
Manufacturers might chemically cross-link biologic devices to decrease the immune response to foreign tissue. However, chemical cross-linking has been shown to result in chronic inflammation,[9] encapsulation, and even a host-versus-graft type of reaction.[2] Lastly, chemical cross-linking might be performed to increase the strength of the biologic device. Yet this is not always the case. At least one study has shown that cross-linked porcine dermis actually decreases in strength of incorporation after two weeks and beyond (see Figure 2 below).[10]

Biodesign is not chemically cross-linked

Because it is not chemically cross-linked during the careful treatment process, Biodesign provides a natural scaffold that allows the body to restore itself through site-specific tissue remodeling. As healing occurs, Biodesign initially acts as a scaffold material to support the population of the ECM with patient-derived cells. Over time, Biodesign is gradually remodeled and integrated into the body, leaving behind organized patient tissue that provides long-term strength.[11] Biodesign grafts are not cytotoxic, are resistant to infection and encapsulation, and become strong, vascularized tissue that functions naturally. As shown in Figure 2, Biodesign grafts result in a repair that becomes stronger over time.[10]

This revolutionary tissue-repair technology is available for use in many parts of the body. As of June 2020, more than 1,600 journal articles have been published about the technology on which Biodesign is based, including long-term data.[11] Biodesign is a breakthrough advancement in the evolution of tissue repair—a whole new category.

Figure 2: Strength of incorporation (SOI)



Strength of incorporation of explanted grafts. Days post-implantation versus tensile strength in megapascals (MPa). Error bars = SEM, N=6.[10]

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