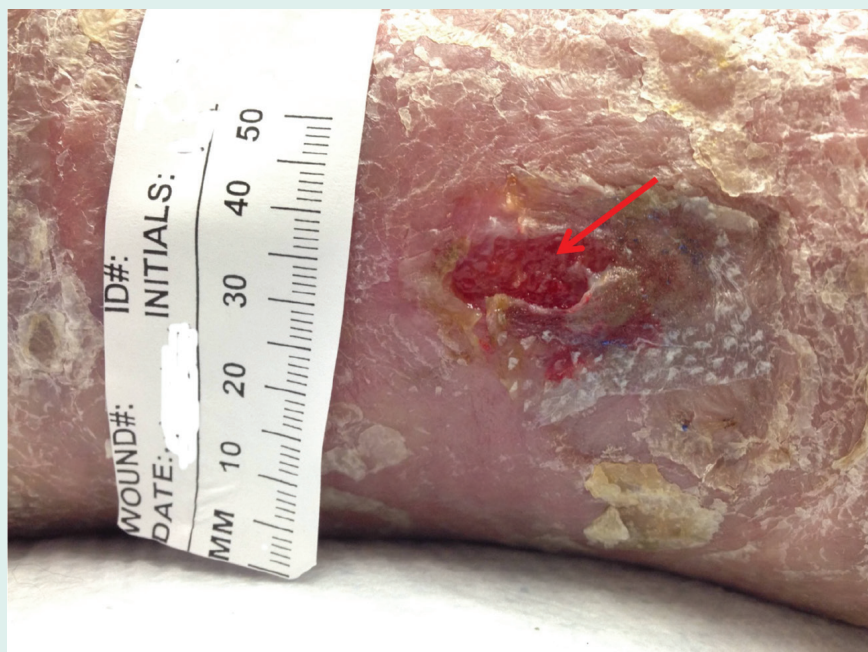


# Endoform: A Simple Tool to Assess Wound Proteases

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Wound proteases (eg, matrix metalloproteinases) are present in both acute and chronic wounds; they are involved at every phase of wound healing, playing a pivotal role in maintaining tissue extracellular matrix (ECM) when balanced with their natural inhibitors. A chronic wound doesn't progress normally through the stages of healing and is characterized by high levels of wound proteases. Chronic wounds stall in the inflammatory phase of healing due to elevated proteases that cause sustained degradation of tissue ECM and inactivation of growth factors and cellular receptors. This disrupts the balance between tissue breakdown and repair. Until wound protease balance is restored, a state of constant ECM breakdown persists and healing is halted.

Endoform (Aroa Biosurgery Limited, Auckland, NZ; marketed in the United States by Appulse, New Haven, CT) is unique within the collagen dressing category because it contains intact natural ECM. Just like tissue ECM, Endoform is susceptible to wound proteases. When wound protease concentrations are excessive, Endoform's ECM is digested and new tissue ECM is unable to form (see Figure 1). The high levels of proteases continually degrade the native ECM built by wound fibroblasts. As wound proteases are reduced with Endoform use, fibroblasts can build an ECM that will persist and not undergo digestion and degradation. As residual Endoform is observed in the wound, balance is being restored and healing can occur (see Figure 2). Balancing excessive protease activity



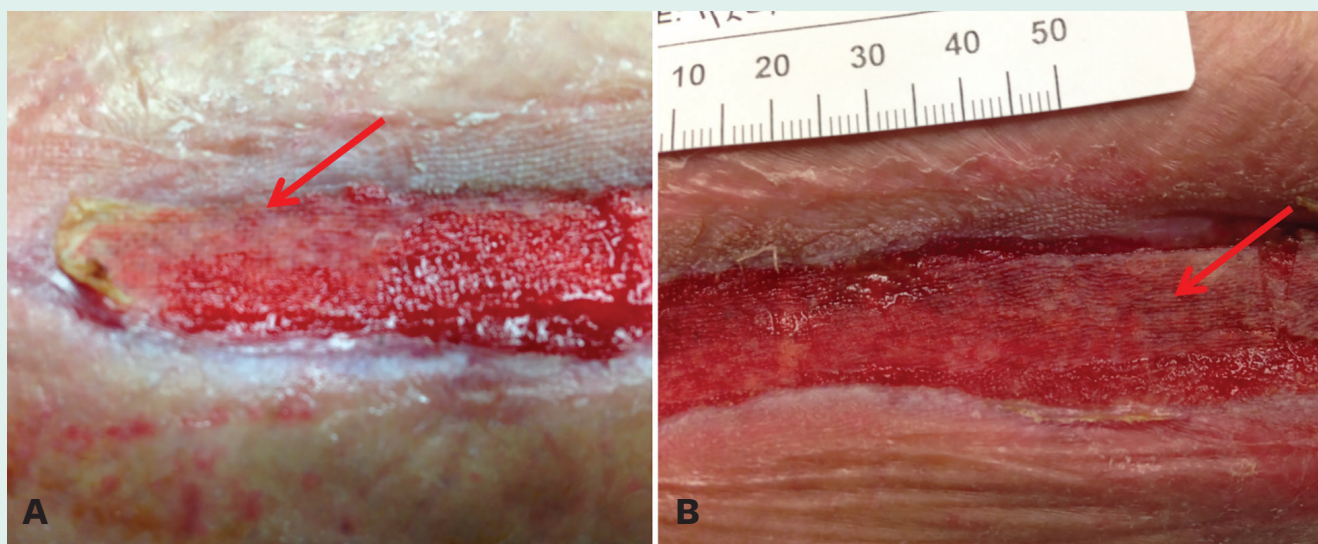
**FIGURE 1.** Endoform extracellular matrix is consumed by protease activity. Endoform remains outside the margin of the wound.

allows the wound to transition from the inflammatory to the proliferative phase of healing and go on to closure. Traditional reconstituted collagen dressings can act as sacrificial substrates for excessive protease activity; however, these products are not comprised of an ECM. They dissolve or gel in the wound bed and provide no cue as to the state of protease levels.

When my facility started managing chronic wounds using Endoform, we applied a single layer of the product. At the weekly follow-up visit, we often observed Endoform was missing from the wound bed (see Figure 1). Endoform had been degraded due to elevated pro-

tease levels. We concluded Endoform could be used as a visual indicator of protease activity in the wound.

To adequately buffer excessive wound proteases and transition the wound from the inflammatory phase to the proliferative phase, we subsequently managed wounds with layers of Endoform. We concluded that if Endoform remained on the wound when the patient returned for their next clinic visit, we had applied enough to buffer protease concentrations for that interval. Over the course of treatment, we adjusted the amount of Endoform (number of layers) based on the presence or absence of Endoform in



**FIGURE 2.** a) Endoform is no longer consumed and remains in the wound; b) granulation tissue formation is noted. Endoform appears to be incorporating into the wound.

the wound bed (see Figure 3). When we began to see remnants of Endoform (see Figure 2a,b), we knew we had applied enough Endoform to the wound to modulate the proteases and provide a provisional ECM for healing. According to the descriptions of its characteristics, we surmised Endoform was participating in healing (see Figure 2).

We have adopted this strategy using Endoform as a clinical cue. The consumption of Endoform indicates protease activity in the wound. The degradation of multiple layers of Endoform is thought to indicate high levels of proteases. Once residual Endoform was observed in the wound, we concluded proteases had been reduced and balance was being restored. Seeing Endoform remnants indicated the transition from the inflammatory to the proliferative phase of healing. Endoform was participating in the development of granulation tissue and sticking to the wound surface. Using these clinical cues, we can assess the protease levels in the wounds we manage and apply a sufficient dose of Endoform to treat excessive proteases, using observational cues to adjust effective use of Endoform and more effectively treat chronic wounds and promote healing. ■



**FIGURE 3.** Endoform dosing by layering to ensure at least one layer of dressing remains to buffer protease activity during the treatment period.