and texture of scars in the setting of Mohs complex closures 2 to 3 months after surgery. To our knowledge, this is the first time that this has been demonstrated with a fractional ablative laser or in a prospective study. It is also the first time that this has been demonstrated on nonfacial sites, as shown in the Figure.

Nine of the 10 subjects elected to have treatment of the control side with the laser at follow-up. It is a limitation that both sides of the scar were ultimately treated, which prevents longer-term evaluation.

We have used this method to achieve minimal scarring on face-lift incision lines with excellent results. This work could potentially change the current approach in all surgical disciplines if these results can be validated with a long-term (6-12 months) multicenter study.

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Recent studies have shown that severely damaged cells, such as necrotic cells and apoptotic cells, release high-mobility group box 1 protein (HMGB1), a nonhistone nuclear protein with a dual function. Inside the cells, HMGB1 is a nuclear constituent loosely bound to chromatin, and it plays a role in transcriptional regulation, while outside the cells, HMGB1 serves as an activator of the inflammatory cascade.2,3

Methods. To evaluate a link between HMGB1 and SJS and TEN, we measured HMGB1 levels in serum samples from 22 healthy control subjects (mean [SD] age, 31.2 [4.6] years; 9 men, 13 women), 11 patients with maculopapular drug eruptions (MPEs), 13 patients with EM, and 13 patients with SJS and/or TEN (Table). All diagnoses were based on the classification system proposed previously.4 Disease onset (day 1) in patients with SJS and/or TEN was defined as the day when mucocutaneous and/or ocular lesions occurred. (Of note, we collected the serum samples of SJS and/or TEN before the onset of SJS and/or TEN, when the patients might have been diagnosed as having EM or MPE at the time of the assay, but the patients then developed SJS and/or TEN.) The serum HMGB1 levels were measured with an HMGB1 enzyme-linked immunosorbent assay kit (Shino-Test Co, Tokyo, Japan) according to the manufacturer’s protocol. Informed consents were obtained from each patient, and the institutional review board or ethics committee of each institution approved the study protocol.

Results. Serum HMGB1 levels of all healthy control subjects and patients with MPE and EM were lower than 6 ng/mL. In contrast, serum HMGB1 levels in patients with SJS and/or TEN at days −7 to −1, days 1 to 7, and days 8 to 21 after onset were significantly higher than those of both healthy controls and patients with MPE and EM (Figure 1). The sensitivity of the assay for SJS and/or TEN above the threshold level was 45.4%. Consistent with these results, immunohistochemical analysis for HMGB1 with anti-HMGB1 antibody levels (Upstate Biotechnology, Lake Placid, New York) and diaminobenzidine staining demonstrated strong positivity for HMGB1 at the nuclei and perinuclei of keratinocytes in the necrotic keratinocytes in patients with SJS compared with those in healthy donors, suggesting that HMGB1 is present in the extracellular spaces in SJS and/or TEN.

Comment. The role of HMGB1 detected in SJS and/or TEN is unknown. Since HMGB1 serves as an activator of the inflammatory cascade and to attract a wide variety of cells,2,3 HMGB1 induced from necrolytic keratinocytes

![Figure 1](image1.png)

**Figure 1.** Increased serum high-mobility group box 1 protein (HMGB1) levels in patients with Stevens-Johnson syndrome (SJS) and/or toxic epidermal necrolysis (TEN). Serum HMGB1 levels of healthy control subjects, patients with maculopapular drug eruption (MPE), exudativum multiforme (EM), and SJS and/or TEN. In patients with SJS and/or TEN, we examined concentrations of serum HMGB1 during 3 time periods: days −7 to −1 (n=3), days 1 to 7 (n=15), and days 8 to 21 (n=14) by an enzyme-linked immunosorbent assay. *P<.05 between the indicated groups by the Tukey nonparametric multiple comparison test.

![Figure 2](image2.png)

**Figure 2.** Skin samples from a healthy donor (A) and a patient with Stevens-Johnson syndrome (SJS); scale bars indicate 100 µm. A, The skin of a healthy donor. B, Skin from a patient with SJS was immunostained for high-mobility group box 1 protein (HMGB1). Arrows point to highly HMGB1-positive areas at the nuclei and perinuclei of keratinocytes.
may act to stimulate inflammation and/or regeneration of the skin lesions. Increased levels of serum HMGB1 have been reported in several diseases such as severe infection and/or sepsis, trauma, cancers, and systemic lupus erythematosus, which were not observed in our patients with MPE, EM, and SJS and/or TEN.

It has been reported that granulysin and Fas ligand are possible candidates as biomarkers for early diagnosis of SJS and/or TEN, but the duration of elevated granulysin and Fas ligand levels is limited; therefore, false-negative results for SJS and/or TEN could occur. In this regard, HMGB1 levels were high at the early stage of SJS and/or TEN and remained elevated even after the onset, which is in contrast to the kinetics of granulysin and Fas ligand. Although the numbers of patients with SJS and/or TEN were limited in this study, we propose that measurements of HGMB1 in combination with granulysin and/or Fas ligand would be a useful diagnostic tool for cases of SJS and/or TEN that require early diagnosis and treatment.

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**14-MHz Ultrasoundography as an Outcome Measure in Morphea (Localized Scleroderma)**

The determination of therapeutic efficacy in morphea (aka, localized scleroderma) is difficult owing to a lack of validated outcome measures. Outside of the United States, 20- to 25-MHz ultrasonography has demonstrated its validity, reproducibility, and responsiveness to change. Preliminary studies on the lower-frequency ultrasonography available in the United States (10-15 MHz) demonstrate that it may have similar attributes. However, studies correlating ultrasonographic findings with lesion stage (inflammatory, sclerotic, or atrophic), clinical scoring systems, or histologic traits have not been conducted.

**See Practice Gaps at end of letter**

Methods. We identified 14 patients with 16 morphea lesions (Table) from the University of Texas Southwestern Medical Center Morphea Registry and DNA repository. Each patient and lesion was assessed for morphea subtype and clinical stage and was assigned a Modified Rodnan Skin Score (mRSS) by a single board-certified dermatologist (H.T.J.).

A single site for ultrasonography and biopsy, as well as a control site, was chosen by the dermatologist and marked with a surgical pen. Ultrasonographic examination was performed by 2 radiologists blinded to the results of the clinical assessment of each patient. Each lesion had dermal thickness measured and ecchogenicity determined as compared