

Original Article

A Consensus-Based Clinical Activity Score (CAS) Atlas for Thyroid Eye Disease in East Asian Patients: A KSOPRS Initiative

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Abstract

Purpose: To develop a consensus-based photographic atlas tailored to East Asian patients to improve the consistency and clinical applicability of the Clinical Activity Score (CAS) in thyroid eye disease (TED), while maintaining compatibility with the established CAS framework.

Methods: Under the auspices of the Korean Society of Ophthalmic Plastic and Reconstructive Surgery (KSOPRS), an expert Atlas Committee comprising eight TED specialists curated representative clinical photographs corresponding to the five sign-based CAS items: eyelid swelling, eyelid erythema, conjunctival redness, conjunctival swelling, and inflammation of the caruncle or plica. Images were categorized as CAS-positive or CAS-negative following multiple rounds of expert review and discussion. The finalized atlas was circulated to all KSOPRS members for consensus approval.

Results: The atlas provides standardized photographic panels and concise operational guidance for each sign-based CAS item. East Asian-specific considerations, including thicker eyelid skin, fuller preseptal and septal fat, and epicanthal folds, are incorporated to refine interpretation of inflammatory signs that may appear attenuated compared with photographic references derived from white populations of European ancestry. The atlas emphasizes pattern recognition, distribution of findings, and side-to-side comparison rather than absolute intensity of erythema or swelling, aiming to reduce false-negative judgments and improve inter-observer consistency.

Conclusions: This ethno-specific standard photographic atlas enables endocrinologists and ophthalmologists to perform rapid and reproducible assessments in outpatient settings, facilitating the early identification of patients requiring referral or urgent treatment.

Keywords: Clinical activity score; East Asian; Ethno-specific standardization; Photographic atlas; Thyroid eye disease

INTRODUCTION

Thyroid eye disease (TED) or Graves' orbitopathy is an autoimmune condition requiring timely management. However, it is difficult to evaluate TED consistently. The Clinical Activity Score (CAS) was proposed in 1989 to evaluate disease activity in TED [1], and has since been refined through multiple validations and confirmations [2,3]. Over the past two decades, the European Group on Graves' Orbitopathy (EUGOGO) has adopted the CAS as a key standard for assessing disease activity and developed management guidelines for thyroid eye disease based on this framework [4-7].

CAS remains a widely used pragmatic framework for describing inflammatory activity in clinical settings. CAS is valued for being simple, clinical, and implementable without specialized equipment; however, its application depends on how examiners recognize and document inflammation signs. The photographic approach was validated. A 2024 international study using photograph-based assessment showed excellent inter-rater reliability for inflammation and motility restriction, supporting the reproducibility of visual sign evaluation across raters [8]. Because CAS relies on sign-based judgments, anchoring it with standardized photographic exemplars is well positioned to deliver consistent and scalable activity assessment in practice.

A recent nationwide survey in Korea reported widespread use of CAS and EUGOGO severity classifications in routine practice [9]. Recent studies from East Asia have highlighted significant differences in TED clinical presentation, severity, and phenotypic features among East Asian populations compared with white populations [10-13]. However, most photographic examples and teaching materials that clinicians worldwide rely on were developed predominantly from white populations of European ancestry [3,7,14]. Reliance on white population-derived exemplars may limit the recognition and optimal management of TED in non-white populations, underscoring the need for region-specific educational resources and diagnostic criteria. This gap is increasingly recognized in the literature, with calls for more inclusive materials that reflect the diversity of TED presentations globally [15,16]. In this context, and because most patients in our setting are East Asian, the present work provides East Asian-appropriate reference images while keeping the CAS framework unchanged. This approach preserves compatibility with existing guidelines and practice patterns while supplying visual anchors that are better matched to patients seen in East Asian clinics.

METHODS

Scope and approach

This article deliberately does not propose a new scoring system, modify item definitions, add domains or folds to imaging, or use other adjunctive tools. Instead, we maintained the CAS as used in current practice and offered a sign-based photographic atlas to support more consistent *positive/negative* judgments for items that are assessed visually by definition. Symptom-based items (e.g., spontaneous orbital pain and pain on attempted gaze) and time-change items (e.g., change in proptosis, ocular motility, and visual acuity) remain clinician-elicited and outside the scope of this photographic atlas. Despite recent advances in imaging strategies for TED activity staging [17,18], imaging and other adjunctive tools were beyond the scope of this study. Within this tightly defined remit, this article provides curated photographic panels for each sign-based CAS item, highlighting negative versus positive examples and briefly noting special considerations in East Asian eyes.

Image selection and consensus process

Under the auspices of the Korean Society of Ophthalmic Plastic and Reconstructive Surgery (KSOPRS), a dedicated Atlas Committee was established to develop an atlas of TED. Starting in June 2025, a specialized committee comprising eight TED experts was convened. The members reviewed the representative images and, following multiple rounds of discussion, compiled a comprehensive collection of figures deemed the most characteristic of each CAS item. The Committee decided to categorize each CAS item as only *positive/negative* rather than detailing them further, prioritizing practical applications and universal utility. The committee meticulously selected the most appropriate clinical photographs that best represented the positive and negative features of each CAS category. Subsequently, the finalized materials were circulated to all KSOPRS members (n=271) via email. Members were invited to review them and provide feedback, including any objections, during a one-week circulation period. Only three minor suggestions were received, including two requests for improvement of figure panels and one request for revision of a figure legend. These suggestions were incorporated into the final version. The Institutional Review Board of University Hospital (No. 4-2025-1296) approved the study protocol, which waived the requirement for written informed consent due to the retrospective nature of the study.

CAS framework

This study retained the most recent CAS framework, including its items, definitions, and binary (CAS-positive/CAS-negative) scoring [7]. The photographic atlas focuses on five sign-based items: eyelid swelling, eyelid erythema, conjunctival redness, conjunctival swelling, and inflammation of the caruncle

or plica. Each item was recorded as *either CAS-positive or CAS-negative*. The total CAS is the simple sum of the positive items, as per the standard approach. CAS<3 is considered inactive, while CAS≥3 is considered active in 7-point initial CAS. CAS<4 is considered inactive, while CAS≥4 is considered active in 10-point follow-up CAS. Interpretive thresholds remain largely unchanged from current practices [6,7], with several *East Asian-specific considerations* highlighted in this article.

RESULTS

Following circulation to all KSOPRS members (n=271), no substantive objections were raised, indicating broad agreement, and consensus approval of the finalized atlas was achieved. The atlas presents standardized photographic panels with concise operational notes and East Asian-specific considerations to support consistent interpretation.

Eyelid swelling

Eyelid swelling is defined as diffuse inflammatory swelling of the eyelids (upper and/or lower). The overall contours of the upper and lower eyelids should be inspected with the patient in the primary gaze and the eyelids in a natural, relaxed position. The item is scored as *positive* when there is diffuse, ill-defined puffiness of the pretarsal or preseptal tissues that softens the lid creases and blunts the peri-lid contours (Fig. 1). There are several different forms, including subcutaneous fluid accumulation, lacrimal gland swelling, and dermal/soft tissue thickening. Because eyelid swelling primarily occurs in the preseptal area, shadows often appear along the lateral orbital rim. This feature can help identify typical eyelid swellings.

East Asian-specific considerations

In many East Asian lids, thicker, yellow-hued skin and fuller preseptal/septal fat blunt the visible expression of edema. Erythema may be minimal, and “mild-looking” swelling can represent substantial fluid collection and raised orbital pressure. When there is new onset swelling with loss of crease definition compared with baseline, even if only “mild” and therefore negative by white population-derived exemplars [3,7], it is appropriate to score eyelid swelling as *positive* within East Asian CAS. In practice, such cases often improve with periocular or systemic corticosteroids, which can retrospectively confirm their activity. Accordingly, appearances that would be judged “mild” in white population-derived exemplars are classified as *positive* in this atlas when seen in East Asian lids. Although this represents a

less strict visual threshold than the EUGOGO atlas, it reflects the anatomic differences in East Asian eyelids and was adopted by the KSOPRS through a formal consensus.

Eyelid erythema

Eyelid erythema is defined as erythema of the eyelids compared to the rest of the face and the contralateral eyelid. The overall pretarsal and preseptal areas should be inspected with the patient in the primary gaze and the eyelid in a natural, relaxed position. Evaluation should be performed under adequate lighting because assessment is difficult in dim environments. This item was scored as *positive* when there was a confluent, physiologically plausible redness of the pretarsal/preseptal skin (Fig. 2).

East Asian-specific considerations

Because the skin is thicker and the baseline hue is yellow, erythema often appears muted in East Asian lids. Intensity matching with reference photographs from white populations is not required. The assessment should prioritize confluence and extent, distinguishing diffuse pretarsal or lid-margin erythema from the localized redness of blepharitis. A comparison should be made with the adjacent malar skin rather than with the absolute color. Cosmetic pigment/tattoo lines and dermatitis/rosacea scale are common confounders and should not be misinterpreted as TED erythema.

Conjunctival redness

Conjunctival redness is defined as bulbar conjunctival redness affecting ≥ 1 quadrant. Redness confined to the plica semilunaris or caruncle should be scored under the inflammation of the caruncle/plica items and must not contribute to the conjunctival redness criterion. Redness is frequently localized to the extraocular muscle insertions. Accordingly, assessment should not rely on the primary gaze alone; the bulbar conjunctiva should be examined in the medial and lateral gaze to visualize the nasal and temporal insertions. Superior limbic keratoconjunctivitis (SLK) is frequently observed in patients with TED and is sometimes regarded as an important sign suggestive of severe TED or as a prognostic factor [19,20]. Therefore, the examination should include the elevation of the upper eyelid during downgaze to assess the superior limbus and detect SLK-type injections, which are otherwise easily overlooked. The examination should also include elevation of the upper eyelid with downgaze to assess the superior limbus and detect SLK-type injections, which are otherwise easily overlooked. The item is scored as *positive* when the bulbar vessels are dilated and branched over at least one quadrant (superior, inferior, nasal, or temporal)

(Fig. 3). However, perilimbal flushes are insufficient. Conjunctival hyperemia caused by other conditions, including pterygium, pinguecula, and allergic conjunctivitis, should be differentiated. Chronic SLK alone may not indicate conjunctival redness caused by TED. Therefore, in such cases, the clinical findings should be carefully evaluated in conjunction with the patient's history. When the patient's medical history and other clinical findings are considered comprehensively, the patient may be assigned as CAS-positive for this item based on the presence of SLK.

East Asian-specific considerations

Conjunctival redness showed no significant clinical differences in frequency or severity between East Asian and white populations, and its presentation was comparable to that illustrated in the EUGOGO atlas.

Conjunctival swelling

Conjunctival swelling (chemosis) is defined as a significant fluid collection underneath the bulbar conjunctival layer. The item is scored as *positive* when the total height of fluid collection underneath the bulbar conjunctiva is more than one-third of the palpebral aperture or when the conjunctival swelling protruded beyond the gray line of the lower eyelid (Fig. 4). Conjunctival swelling typically appears elevated, translucent, and gelatinous, protruding beyond the limbal curvature, or forming fluid-filled folds over the sclera in the primary gaze. Significant conjunctival swelling was observed in the severe cases. One study found that thyroid-stimulating immunoglobulin levels were significantly higher in patients with chemosis than in those without [21]. Conjunctival swelling occurs less frequently than eyelid swelling and conjunctival injection [13,22,23]. This suggests that even among the signs of CAS, the presence of chemosis may be an indication of very high disease activity. Chemosis typically occurs in the lower quadrant of the conjunctiva, often due to exposure when the eye cannot be closed completely. Vertical manipulation of the lower eyelid and inspection of the lateral conjunctiva helps identify mild chemosis. Accuracy improves with slit-lamp examination. A thin vertical beam (45°-60° incidence) from the lateral canthus toward the limbus allows for an accurate assessment of the divergence of the reflected column. Conjunctivochalasis, which settles with downgaze and lacks the glassy edema characteristic of chemosis, should be differentiated. A thick tear meniscus caused by reflex tearing in dry eye patients may mimic conjunctival swelling and should not be misinterpreted as chemosis. If chemosis is isolated (other CAS parameters are negative), TED-unrelated causes, such as lagophthalmos or recent drop-related ballooning, should be considered before attributing to activity.

East Asian-specific considerations

If the conjunctival swelling is isolated then postoperative eyelid complications that are relatively common in East Asian practice, such as prior cosmetic lateral canthoplasty or lower eyelid blepharoplasty, should be considered.

Inflammation of caruncle/plica

Inflammation of the caruncle/plica is defined as swelling and redness of the caruncle or plica semilunaris. While primary gaze assessment suffices in most cases, the plica is better seen in lateral gaze at the medial canthus. Diagnostic accuracy improves with slit-lamp examination, which assesses surface microcontours and hyperemia. The item is scored positive when the caruncle/plica showed edema or hyperemia beyond usual prominence, with a beefy or gelatinous appearance obscuring normal sulci in the medial canthus (Fig. 5). Protrusion of the caruncle or plica with closed eyelids was an unequivocally positive finding.

The caruncle is a transitional zone between the skin and conjunctiva that contains adnexal structures such as hair follicles and sebaceous glands. Swelling of the plica was more common than that of the caruncle. Inflammation of the caruncle and plica is typically observed in cases of high CAS and marked congestion, and caruncular swelling due to lagophthalmos may persist. Therefore, ensuring proper eyelid closure is important.

East Asian-specific considerations

Epicanthal folds are common in East Asians, and many individuals have indistinct lid creases, resulting in less exposure of the caruncle compared to white populations. Consequently, caruncular swelling appears to be less frequent. However, no comparative studies have been conducted to date, and further investigation is warranted.

DISCUSSION

Addressing the limitations through ethno-specific standardization

This atlas addresses the limited applicability of current photographic exemplars, derived mainly from white European populations, to East Asian patients. The study followed the CAS framework, retaining binary scoring while introducing East Asian-specific considerations to refine clinical judgment and

improve diagnostic consistency.

Anatomical differences require a refined approach. In East Asian eyelids, features such as thicker, yellow-hued skin and fuller preseptal/septal fat can dampen the visible expression of erythema and make true inflammatory swelling appear deceptively "mild." Our atlas helps the examiner avoid false judgements by providing reference exemplars that prioritize pattern and distribution over mere intensity of color or swelling. The standardization provided by this atlas, which focuses on improving the consistency of *positive/negative* judgments for visually assessed items, is anticipated to reduce ambiguity at the point of care and improve inter-observer agreement, thereby facilitating comparability across different centers.

Value of early diagnosis and appropriate treatment

The most practical benefit of this simplified and standardized atlas is its potential to improve early diagnosis and management of TED. In TED, early intervention is essential. Early treatment of TED, particularly within the first six months of symptom onset, is associated with an improved response to systemic steroids and radiotherapy [7,24]. Multiple meta-analyses and consensus guidelines have demonstrated that interventions during the initial active phase of TED result in greater reductions in clinical activity scores, proptosis, and diplopia than treatment initiated during the chronic phase [25,26]. Conversely, delayed referral or treatment increases the risk of severe, sight-threatening complications [7,24,27].

As a triage tool and the role of the endocrinologist

Crucially, this atlas is designed to support not only ophthalmologists but also endocrinologists, who serve as the primary points of contact for patients with Graves' disease. It is important for endocrinologists to possess basic ophthalmologic evaluation skills for patients with Graves' disease because early recognition of TED enables prompt intervention, which is associated with improved visual and functional outcomes [28,29]. The ATA-ETA consensus statement emphasizes that endocrinologists should assess the signs related to TED and urgently refer to these signs [7]. However, the current CAS framework is somewhat complex and often require ophthalmologic equipments. Accordingly, this study has streamlined and systematized it as succinctly as possible. By providing a clear, visually standardized tool for assessment of East Asian patients, we aimed to bridge the gap between endocrine management and specialized ophthalmology care, leading to earlier therapeutic interventions and, ultimately, better patient outcomes.

Clinical integration of activity assessment, serology, and imaging

Non-CAS activity metrics like imaging-based metrics and serologic results have gained emphasis in current practice [17,18,30-38]. The CAS is a clinical evaluation tool, and management decisions should integrate CAS findings with other clinical indices [39]. Management should be guided by a comprehensive ophthalmologic evaluation that incorporates visual function, structural findings, and overall disease severity. In this framework, photo-anchored CAS assessment helps standardize the evaluation of inflammatory activity, while clinical, serologic, and imaging findings inform treatment escalation, tapering, and peri-operative decision-making. Korean practice patterns further emphasize TSH-R antibody assays and cross-sectional imaging for evaluating extraocular muscle enlargement, apical crowding, and alternative diagnoses [9].

Low-CAS, high-severity phenotype in East Asian patients

The need for an accurate assessment in East Asian populations is underscored by reports of phenotypic differences and evidence that some cohorts show a higher prevalence of low CAS but progressively severe disease [10-13]. In this phenotype, overt inflammatory signs are muted; however, serious orbital consequences such as severe proptosis or dysthyroid optic neuropathy may still develop [10-12]. Accurate activity assessment is critical because the early active phase determines the responsiveness to systemic steroids and radiotherapy. Conversely, a low CAS in a non-standardized context risks misclassifying a truly active disease as quiescent, which can delay treatment and lead to irreversible complications. To mitigate this, the present atlas adopts a slightly more sensitive threshold than the conventional CAS exemplars for detecting changes and classifying findings as positive. For low-CAS but high-risk presentations, early imaging of the extraocular muscles and orbital apex should be prioritized, rather than evaluation based on minimally positive visual signs alone. Therefore, clinicians should not rely solely on the atlas but should also carefully assess symptom changes through detailed history taking.

Limitations of this atlas

The main concern of this atlas is that images drawn primarily from Korean patients may not represent 'East Asian' broadly. While this atlas uses 'East Asian' as a primary descriptor, we acknowledge the phenotypic diversity within East Asia. Given this limitation, this atlas is presented as a first pragmatic

step toward multi-country East Asian coverage, rather than a final pan-East Asian standard. To maximize practical use, the atlas was simplified and kept close to the existing CAS framework. However, this simplicity may overlook subtle distinctions captured by conventional CAS.

Future directions

Future guidance should clarify how CAS-based visual assessments can be combined with other non-CAS clinical indices in East Asian clinical practice. Lower eyelid retraction, acquired epiblepharon, corneal erosions, milder proptosis are more commonly identified clinical features in East Asian patients with TED compared to white populations [13,40]. Beyond the CAS visual signs proposed in this study, other clinical indices influenced by East Asian-specific phenotypic features may also warrant consideration, suggesting the need for East Asian-specific guidelines.

This evidence base warrants further strengthening. A brief, practical inter-rater reliability study across East Asia using this atlas in endocrinology and ophthalmology clinics would help quantify gains in agreement and identify image panels that require refinement.

Research on deep learning–based activity assessment in TED is advancing, and an East Asian reference image set, such as this atlas, is likely to play an important role in future work [41-43]. Broadening the ancestry representation by incorporating curated images from other East Asian countries, such as Japan and China, would better reflect the phenotypic heterogeneity within the 'East Asian' population and enhance the generalizability of the atlas.

Taken together, this consensus-based atlas provides a practical visual reference for applying the CAS in East Asian patients with TED while preserving compatibility with the established CAS framework. By anchoring visually assessed CAS items to standardized photographic exemplars that reflect East Asian anatomical characteristics, this resource may support more consistent clinical judgments and facilitate rapid outpatient assessment by both ophthalmologists and endocrinologists. In turn, improved recognition of disease activity may promote earlier referral and more timely therapeutic intervention. Future studies should evaluate inter-observer reliability and validate the applicability of this atlas across diverse East Asian populations.

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Data availability statement

The data are available from the corresponding author on reasonable request.

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Figure 1. Eyelid swelling. (A, B) CAS-negative. There is no prominence or puffiness around the lid crease line, and no shadowed area suggestive of swelling is observed. (C) CAS-positive. Preseptal and pretarsal subcutaneous fluid collection. In Asian patients, this degree of eyelid swelling may be underestimated due to relatively thicker eyelid skin. (D) CAS-positive. Preseptal subcutaneous fluid collection in the upper and lower eyelids. (E) CAS-positive. More pronounced eyelid swelling in the upper and lower eyelid. (F) CAS-positive. Because eyelid swelling mainly involves the preseptal area, a shadow often appears along the lateral orbital rim due to the prominence of edematous eyelid.

Figure 2. Eyelid erythema. (A, B) CAS-negative. There is no noticeable color difference between the eyelid and the surrounding facial skin. (C, D) CAS-positive. A prominent color difference between the upper eyelid skin and the surrounding facial skin is noted. Eyelid erythema is also evident in the lower eyelid skin. There is a definite color difference between the orbital area and the upper nasal area. (E) CAS-positive. Eyelid erythema can be confined to the pretarsal area. (F) CAS-positive. Yellowish skin tone and prominent eyelid fat may obscure eyelid erythema; however, the pretarsal and preseptal areas appear reddish relative to the surrounding yellowish facial skin.

Figure 3. Conjunctival redness. (A, B, C, D) CAS-negative. (E) CAS-positive. The bulbar vessels are dilated and branch along the visible conjunctival surface. (F) CAS-positive. Redness over the rectus muscle insertion area is common. (G, H) CAS-positive. More generalized conjunctival redness is noted. (I, J) CAS-positive. Superior limbic keratoconjunctivitis (SLK) commonly coexists with TED. Careful examination with gentle elevation of the upper eyelid is recommended. When correlated with clinical history and other inflammatory signs, the presence of SLK supports CAS positivity. (K) CAS-positive. Conjunctival redness is predominantly observed over the medial rectus muscle insertion area. Inflammation of the caruncle and plica is also present but should be scored independently. (L) CAS-positive. Conjunctival redness is predominantly observed over the lateral rectus muscle insertion area. Conjunctival redness over the lateral rectus muscle area is a useful indicator for evaluating this item.

Figure 4. Conjunctival swelling. (A) CAS-negative. Conjunctivochalasis without protrusion. The conjunctiva is not prolapsed and the gray line on the lower eyelid remains intact. (B) CAS-negative. Only mild conjunctivochalasis is noted. There is no fluid collection beneath the conjunctiva. A thin vertical beam (45°-60° incidence) from the lateral canthus toward the limbus allows accurate assessment of whether the reflected column diverges. The thin vertical beam remains intact at the junction between the conjunctiva and the lower eyelid. (C) CAS-negative. Minimal fluid collection is noted beneath the

conjunctiva. However, the conjunctival swelling does not protrude beyond the gray line, and the height of the fluid collection is less than one-third of the palpebral aperture. (D) CAS-positive. Marked conjunctival swelling extends beyond the lower eyelid margin, obscuring the gray line. (E) CAS-positive. Marked conjunctival swelling, with the height of the fluid collection exceeding one-third of the palpebral aperture. This degree of conjunctival swelling can be visualized even without a thin slit beam, as evident on gross photographs. (F) CAS-positive. The conjunctival swelling does not protrude beyond the gray line; however, the height of the fluid collection exceeds one-third of the palpebral aperture. (G) CAS-positive. A thin vertical beam (45°-60° incidence) from the lateral canthus toward the limbus allows accurate assessment. There is a fluid collection beneath the conjunctiva. The reflected column of the thin vertical beam diverges, and the height of the fluid collection exceeds one-third of the palpebral aperture. (H) CAS-positive. This degree of conjunctival swelling cannot be easily judged based on the gross photographs alone. Therefore, slit-lamp examination is required. (I) CAS-positive. Slit-lamp photograph of the patient shown in (H). The bulbar conjunctiva is separated from the sclera, and a translucent fluid collection is identified. Darkening the surrounding environment allows more detailed visualization of divergence of the vertical slit-lamp beam. The separation extends to more than one-third of the total height of the palpebral aperture.

Figure 5. Inflammation of caruncle and plica. (A, B, C) CAS-negative. There is no swelling or redness of caruncle or plica. The color of the plica and caruncle is pink or pale pink rather than red. (E, F) CAS-positive. Swelling and redness of the caruncle is more prominent than those of the plica (G) CAS-positive. Swelling and redness of the plica is more prominent than those of the caruncle (H) CAS-positive. Swelling and redness of plica. Inflammation of the plica is more commonly identified than that of caruncle. (I) CAS-positive. Inflammation of the plica. This eye corresponds to the contralateral eye shown in (C). Whereas the plica and caruncle in the opposite eye appear pale pink, the plica in this eye is swollen, and the inferior portion of the plica (indicated by a black arrow) is much more reddish. Such side-to-side comparison can assist in assessing the presence of inflammation. (J) CAS-positive. Prominent swelling and redness of the plica. A beefy or gelatinous appearance obscures normal sulci of the medial canthus.