The development of Favre-Racouchot syndrome (FRS) has been well described in dermatologic literature as having a strong association with chronic sun exposure and ultraviolet damage, which result in the classic appearance of solar elastosis and dilated open comedones in a bilateral periorbital distribution. However, frequently lacking in the literature is mention of another potential risk factor: tobacco use. The authors report a unique case presentation of FRS in a unilateral perioral distribution in a 66-year-old African American female without history of chronic sun exposure, but rather associated with preferential one-sided placement of her cigarettes. It is hoped that this case report will serve to strengthen the evidence that tobacco use may be implicated in the development of FRS.

Abstract
The development of Favre-Racouchot syndrome (FRS) has been well described in dermatologic literature as having a strong association with chronic sun exposure and ultraviolet damage, which result in the classic appearance of solar elastosis and dilated open comedones in a bilateral periorbital distribution. However, frequently lacking in the literature is mention of another potential risk factor: tobacco use. The authors report a unique case presentation of FRS in a unilateral perioral distribution in a 66-year-old African American female without history of chronic sun exposure, but rather associated with preferential one-sided placement of her cigarettes. It is hoped that this case report will serve to strengthen the evidence that tobacco use may be implicated in the development of FRS.

Introduction
Favre-Racouchot syndrome (FRS) has been estimated to affect up to 6% of individuals over the age of 50 and presents most commonly in Caucasian males. It has been well established by past literature that the development of the condition possesses a strong association with history of exposure to solar radiation and actinic damage. Indeed, in addition to the presence of solar elastosis, one of the hallmark characteristics of the disease, numerous periorbital open comedones, have been referred to specifically as "solar comedones." FRS has also been described in a patient following cancer radiation treatments, thought to result from similar pathogenesis involving the interruption of keratinization of the pilosebaceous follicle. Yet, the exact pathogenesis of this disease remains poorly understood, as does the potential for other significant contributive or causative factors.

The authors attempt to demonstrate a rarely emphasized association of the development of Favre-Racouchot Syndrome with long-term tobacco use as described in a unique case presentation. So far, there have been very few but significant publications that have investigated the association of skin changes consistent with FRS and smoking. This case report is noteworthy due to the unique presentation of the patient, who had no other major risk factors for the development of FRS and who also had skin changes that were consistent with the perioral location of her tobacco habit. It is hoped that this article will emphasize that FRS, which is most often thought to result from solar/UV-induced damage, is undoubtedly a disease of multifactorial origin with a potentially strong association with tobacco use.

Case Report
A 66-year-old African American female with history of considerable cigarette use presented with a skin eruption, which she described as "brown bumps," under the right side of her mouth for eight months’ duration. She had previously sought treatment by her primary care physician. Although she denied any history of herpes labialis, she had been treated presumptively with a course of oral acyclovir, resulting in no improvement in appearance. The lesions were asymptomatic but aesthetically displeasing to the patient, and therefore she sought further treatment by a dermatologist.

The patient denied use of hormone replacement therapy, lithium, or epidermal growth factor receptor inhibitors. Furthermore, she denied occupational exposure to halogenated compounds. The patient admitted a 58-year history of cigarette smoking, where she preferentially and incessantly held the cigarette on the right side of her mouth. She denied alcohol consumption or any illicit drug use.

On physical exam, the patient was a well-developed, well-nourished female with Fitzpatrick skin type V. Inspection of the right lower cutaneous lip revealed small cysts and open comedones in an agminate arrangement (Figure 1). There was mild hyperpigmentation but no associated solar elastosis. The remainder of the facial skin, including the periorbital region, was free of similar findings.

A shave biopsy was obtained and demonstrated two mildly inflamed comedonal cysts embedded in a dermis with evidence of severe nodular solar elastosis (Figures 2 and 3). Despite the unusual location and lack of chronic actinic damage, a diagnosis of Favre-Racouchot syndrome was made on the basis of clinicopathologic findings. The patient was treated topically with tretinoin 0.04% gel and counseled on smoking cessation. At three-month follow-up, she reported mild improvement in appearance of the perioral cysts and comedones.

Figure 1. Small cysts and open comedones in an agminate arrangement post shave biopsy.

Figure 2. Photomicrograph of skin containing two mildly inflamed comedonal cysts embedded in a dermis with evidence of severe solar damage (4x).

Figure 3. Photomicrograph of the surrounding dermis demonstrating severe nodular solar elastosis indicating significant prolonged sun exposure (20x).
Discussion

The relationship of FRS with smoking has been investigated in the past, but not to a large extent. Acting on a hypothesis based on clinical experience, one dermatology clinic performed a retrospective study that revealed a statistically significant association between FRS and chronic tobacco use. Furthermore, the authors found the likelihood of developing FRS was dose-dependent when comparing heavy versus light smokers. Drawing on this study’s conclusions, a subsequent publication asserted that smoking holds a stronger association with development of FRS than ultraviolet radiation. Despite this contention, FRS continues to be regarded as a predominantly sun-damage-induced disease process, and these authors could find no further studies investigating the relationship between smoking and FRS development.

This particular case presentation is noteworthy due to the unique nature of a unilateral perioral distribution of the disease, thought to be a direct result of the habitual preference of the patient to hold her lit cigarettes in her ipsilateral mouth. In support of this assumption, changes in the elastic tissue of non-sun-exposed areas in smokers that resemble the histological findings of solar elastic tissue resulting from sun damage have been described. Past in vitro studies have indicated that tobacco-smoke extract impairs the production of collagen and increases the production of tropoelastin and matrix metalloproteinases, which in turn degrade matrix proteins and cause an abnormal production of elastosis material. Moreover, as the patient in this case report is African American, her skin possesses a higher concentration of melanin, which has been shown to be negatively associated with the development of UVR-induced solar elastosis. Complicating the picture is whether exposure to tobacco smoke is solely responsible for the development of the elastosis found in this patient or if the potential long-term exposure to heat (infrared radiation) from the lit cigarette also has impact. One study investigated this question, exposing a group of albino guinea pigs to UVA and UVB radiation with and without infrared radiation. The study found that the combination of UV and IR radiation resulted in dense, mat-like elastic fiber depositions that exceeded what was observed in either source of irradiation alone.

In addition to elastosis, other common histological findings of FRS include epidermal atrophy, basophilic degeneration of the upper dermis, and a decrease in the size of the sebaceous glands with dilated and keratin-filled pilosebaceous infundibulum. As to the unilateral distribution of the patient’s disease, albeit rare, unilateral temporal and periorbital presentations of FRS have been reported in the past linked with occupations involving chronic asymmetrical sunlight exposure. No similar reports of FRS in a unilateral, perioral distribution could be found, despite an extensive literature search. It is unclear why more individuals do not develop the skin findings this patient presented with, as tobacco use is still ubiquitous today despite widespread knowledge of many potential harms. Ultimately, sufficient research on the development of FRS is lacking, and further clinical studies should be performed to gain a better understanding of the pathogenesis and disease factors.

In reference to treatment, although benign, FRS can be aesthetically troubling to patients and has proved challenging to remedy. There have been many proposed therapeutic modalities, including direct extraction, topical or oral retinoids, chemical peels, and microdermabrasion, as well as investigations utilizing CO2 laser that have resulted in good outcomes.

Conclusion

It is hoped that the information presented in this case report will encourage providers to acknowledge that emphasizing smoking cessation in patients is also an essential adjunct treatment for the resolution of FRS and prevention of the disease process.

References