# Elucidating the pulsed-dye laser treatment of sebaceous hyperplasia in vivo with real-time confocal scanning laser microscopy

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**Background:** Several case reports document successful treatment of sebaceous hyperplasia with the pulsed-dye laser. Moreover, noninvasive real-time confocal laser scanning microscopy elucidates the vascular nature of these lesions and their pathophysiologic response to treatment mediated by vessel coagulation.

**Methods:** Ten patients with 29 lesions of sebaceous hyperplasia were treated with 3 stacked 5-mm pulses of the 585-nm pulsed-dye laser at fluences of 7 or 7.5 $J/cm^2$. Confocal imaging was performed before and immediately after treatment, as well as at 2, 4, and 8 weeks of follow-up.

**Results:** The great majority of lesions responded to one treatment, with complete disappearance in 28%, decrease in diameter in 66%, and flattening in 93%. Although 28% recrudesced after initial involution, only 7% recurred completely. Three lesions became eroded or crusted, and 7 experienced cutaneous depressions before complete healing, but no scarring or pigmentary side effects were noted. Confocal imaging revealed a prominent "crown" of blood vessels surrounding the sebaceous duct and coagulation of these vessels with pulsed-dye laser treatment. However, the vessels reappeared during follow-up, and no noticeable morphologic changes in the sebaceous duct were noted.

**Conclusion:** Vascular targeting of sebaceous hyperplasia can be monitored with real-time reflectance confocal microscopy. Most sebaceous hyperplasia regresses after one treatment with 3 stacked pulses of the 585-nm pulsed-dye laser. Whether this response is due to temporary ischemia induced by selective vessel destruction or nonspecific thermal diffusion beyond the vessels from pulse stacking has not been determined. (J Am Acad Dermatol 2000;43:49-53.)

Sebaceous hyperplasia is characterized histologically by multiple hyperplastic sebaceous gland lobules emptying into a central enlarged sebaceous duct. Despite their large size, often 10 times the size of normal sebaceous glands, these lesions secrete very little sebum. They contain mostly small, undifferentiated sebocytes with large nuclei and scant cytoplasmic lipid, in contrast to normal sebocytes, which become engorged with lipid. The primitive cells in sebaceous hyperplasia move to the central duct more slowly, thus crowding in the gland lobule and inflating its size.[1]

Clinically, sebaceous hyperplasia appears as round, yellow, lobulated papules, several millimeters in size, with central umbilication. Often, they are strikingly telangiectatic, resembling basal cell carcinoma in some lesions. They occur alone or in groups in highly sebaceous areas such as the forehead, nose, and cheeks, arising in early or middle adulthood and increasing in number with age.[1,2] They appear in larger numbers and earlier in immunosuppressed persons, in familial cases, and in certain genodermatoses such as Muir-Torre syndrome and pachydermoperiostosis.[3-5]

Standard treatments for sebaceous hyperplasia include electrodesiccation, curettage, cryosurgery, and topical bichloracetic or trichloracetic acid. In one patient, cryosurgery with a cotton-tipped applicator for 10 to 15 seconds induced clearing of lesions without recurrence, scarring, or hypopigmentation.[2] In 20 patients, topical bichloracetic acid, although
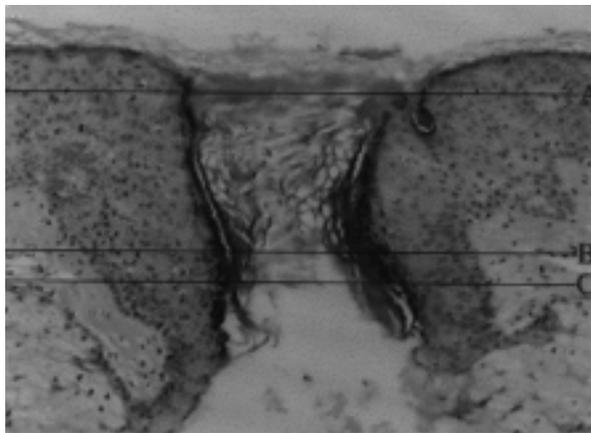
**Fig 1.** Histopathologic features of sebaceous hyperplasia, vertical section. (Hematoxylin-eosin stain; original magnification ×10, 0.25 numerical aperture, dry objective lens.) Dilated sebaceous duct plugged with keratin and sebum empties directly to epidermal surface. Blood vessels surround duct at level of papillary dermis. Large sebaceous lobules beneath empty into duct. *Lines A, B,* and *C* represent depths in epidermis corresponding to horizontal sections in Fig 2.

similarly successful without recurrence, was complicated by prolonged stinging and subtle atrophic scarring.[6] Any nonspecific destructive modality incurs the risks of scarring or dyspigmentation. In patients with numerous lesions, oral isotretinoin has proven successful, with rapid clearing of lesions within 2 to 6 weeks.[4,5,7] However, lesions recurred when the isotretinoin was discontinued, requiring maintenance doses in the range of 10 to 40 mg every other day or 0.05% isotretinoin gel.[4,5,7]

Laser treatment of sebaceous hyperplasia was first accomplished by means of the nonspecific coagulative effect of the argon laser, with good results in 5 cases.[8] More recently, Schönermark, Schmidt, and Raulin[3] used the 585-nm pulsed-dye laser to target the telangiectatic component of these lesions. Two patients were treated with fluences of 6.5 to 8 J/cm² with the 5-mm spot size, experiencing reduction of their lesions after the first treatment and clearing after 1 or 2 additional treatments. No recurrence or scarring was evident after 9 months of follow-up.

Our group reported a single case of sebaceous hyperplasia successfully treated with two stacked 5-mm pulses with the 585-nm pulsed-dye laser at 7 J/cm² without pigmentary changes or scarring. This case report elucidated the pathophysiologic response to treatment with noninvasive in vivo confocal scanning laser microscopy (CM) to obtain noninvasive and repeated images of the lesion before and after treatment. Pretreatment images revealed an infundibular sebaceous duct with hyperplastic epithelium and prominent surrounding vasculature in the form of a "vascular crown." Images taken immediately after treatment confirmed photothermal damage confined to these vessels, and 2-week and 2-month follow-up imaging demonstrated a smoothing of the hyperplastic epithelium lining the infundibular duct.[9]

CM operates by tightly focusing a laser beam on a specific point in the skin, detecting only the light reflected from the focal point through a pinhole-sized spatial filter.[10,11] The beam can then be scanned horizontally over a two-dimensional grid to yield a horizontal section, and the focal length can be adjusted to image successive horizontal planes stacked vertically. Because of significant absorption of light by the skin, imaging is restricted to 300 to 400 µm in depth, with visualization of the epidermis and papillary dermis. The lateral resolution of 0.5 to 1 µm and axial resolution (section thickness) of 2 to 5 µm yield images of histologic quality, with cellular and subcellular detail. Moreover, CM obtains images at a video rate of 10 to 20 Hz, facilitating the visualization of dynamic processes such as blood flow.[12,13] Neither staining nor photochemical reactions are necessary, allowing repeated imaging of skin in vivo without altering the tissue itself.[10-14]

To further investigate the effects of pulsed-dye laser therapy on sebaceous hyperplasia, we conducted a larger study of 29 lesions in 10 patients, using real-time reflectance CM to evaluate the pathophysiologic changes that occur with treatment.

## METHODS

Ten patients with sebaceous hyperplasia were enrolled in the study after signed informed consent. They included 6 men and 4 women from 30 to 57 years of age, with Fitzpatrick skin type I-III. Pretreatment evaluation included a relevant history, examination of the facial skin, and evaluation of the size and elevation of each sebaceous hyperplasia. Photographs were taken with a 35-mm camera, and confocal imaging was performed on an accessible lesion by means of a commercially available, near-infrared, reflectance confocal laser scanning microscope (Vivascope 1000, Lucid Inc, Henrietta, NY). This device uses a diode laser at 830 nm with a power less than 26 mW. The 30× objective lens of numerical aperture 0.9 was applied to the skin with either water (refractive index 1.33) or gel (refractive index 1.3335) used as an immersion medium. Further details of this system have been recently reported.[13]

Between 1 and 7 lesions were treated for each patient, resulting in a total of 29 treated lesions. The 585-nm pulsed-dye laser (Candela Corp, Wayland,
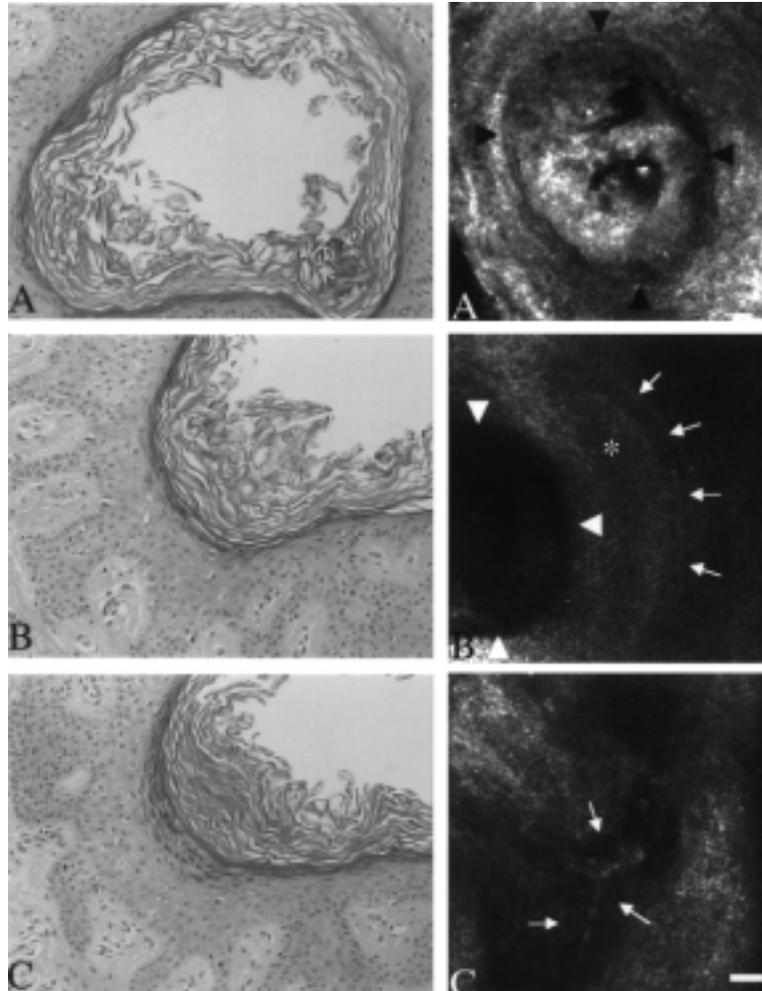
**Fig 2.** Horizontal sections of sebaceous hyperplasia from depths in epidermis corresponding to lettered lines in Fig 1. These were obtained by conventional histopathology (*left,* hematoxylin-eosin stain; original magnification ×10, 0.25 numerical aperture, dry objective) and CM (*right,* original magnification ×30, 0.9 numerical aperture, water immersion, scale bar = 25 μm). **A,** In epidermis, dilated sebaceous duct (*arrowheads*) contains plug of keratin and sebum. **B,** Papillary dermis around sebaceous duct (*arrowheads*) contains vasculature that surrounds duct epithelium (*) like a crown. During confocal imaging, individual blood cells coursing through a circumferential blood vessel (*arrows*) can be seen. **C,** Deeper in papillary dermis are larger blood vessels (*arrows*) in vicinity of sebaceous duct.

Mass) was used to deliver 3 consecutive 5-mm pulses with 7 or 7.5 J/cm² to each lesion treated. Immediately after treatment, confocal imaging was repeated on the previously imaged lesion. Postoperatively, patients applied bacitracin ointment daily until healing was complete. Follow-up examinations were conducted at 2, 4, and 8 weeks after treatment for repeated photography, evaluation of the size and elevation of each treated lesion, and confocal imaging of the one previously imaged lesion. Clinical evaluation of response to pulsed-dye laser was performed by at least two observers.

Confocal images were compared with hematoxylin-eosin–stained sections from a biopsy specimen obtained from one of the subjects before the study.

## RESULTS

The sebaceous hyperplasia lesions treated in this study initially ranged in size from 2 to 8 mm and were distributed over the forehead, glabella, nose, temples, and cheeks. The great majority of lesions responded to one treatment, with complete disappearance in 8 of 29 (28%), decrease in diameter in 19
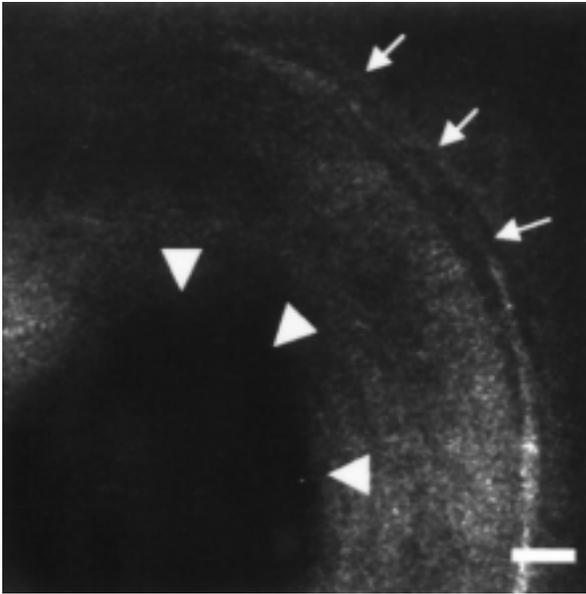
**Fig 3.** Several minutes after pulsed-dye laser treatment, blood vessel (*arrows*) surrounding sebaceous duct (*arrowheads*) contains coagulated blood, which appears refractile and bright (*arrows*). (Original magnification ×30, 0.9 numerical aperture, water immersion objective lens, scale bar = 25 µm.)
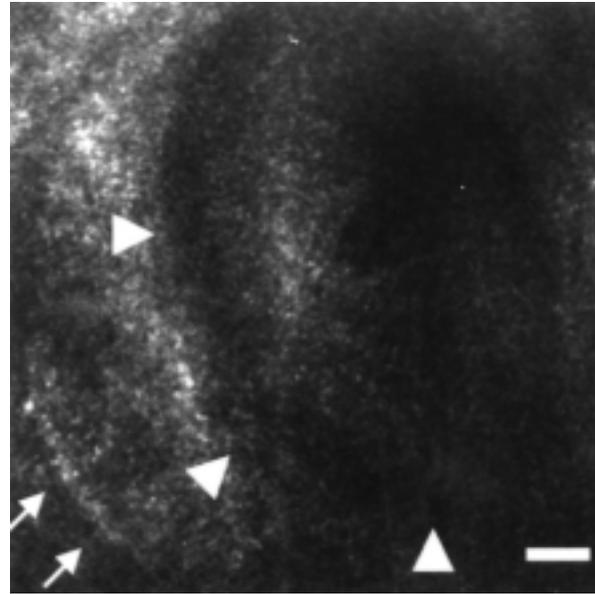


**Fig 4.** Two weeks after pulsed-dye laser treatment, individual blood cells could once again be seen moving through blood vessels (*arrows*) surrounding sebaceous duct (*arrowheads*). (Original magnification ×30, 0.9 numerical aperture, water immersion objective lens, scale bar = 25 µm.)

of 29 (66%), and flattening in 27 of 29 (93%) by the final 8-week follow-up. Before healing, 3 lesions underwent erosion or crusting, and 7 lesions became depressed below the cutaneous surface; only one cutaneous depression remained at the 8-week follow-up. Eight lesions (28%) recrudesced after initial involution, and 2 of these (7%) regained their original sizes. Although neither age, location, pretreatment size, nor fluence (7.0 vs 7.5 J/cm²) influenced the eventual outcome, 8 of 8 lesions that recrudesced were from female patients. No frank scarring or pigmentary side effects were seen.

Fig 1 is shown to exemplify the histopathologic characteristics of a sebaceous hyperplasia lesion in traditional vertical section. The horizontal sections of sebaceous hyperplasia shown in Fig 2 were obtained by means of both conventional histopathology (at left) and real-time CM imaging (at right) at several depths below the surface. A dilated sebaceous duct opening directly to the epidermal surface and containing a plug of keratin and sebum was a common feature (Fig 2, *A*). At the level of the papillary dermis, a "crown" of blood vessels surrounds the sebaceous duct (Fig 2, *B*). Deeper in the dermis, dilated blood vessels could be found in the vicinity of the duct (Fig 2, *C*). The enlarged sebaceous lobules were too deep to be visualized by CM.

Several minutes after pulsed-dye laser treatment, the vessels surrounding the sebaceous duct were replaced by amorphous, refractile cords of coagulated material (Fig 3). Follow-up images obtained at 2 weeks (Fig 4), 4 weeks, and 8 weeks after treatment were not reproducibly or significantly different from pretreatment images, with the exception of 3 patients who demonstrated a temporary absence of keratinocytes overlying the treated lesion at the 2-week follow-up.

## DISCUSSION

This study demonstrates the potential use of CM to noninvasively evaluate dynamic changes after pulsed-dye laser treatment of sebaceous hyperplasia. Moreover, the majority of lesions undergo significant involution after a single treatment with 3 stacked pulses of the 585-nm pulsed-dye laser at moderate fluences, congruent with the success of previous studies.[3,9] As demonstrated previously, it is possible that multiple treatments are necessary for most lesions to achieve complete clearance.[3] However, during the 8-week follow-up period, 8 of 29 lesions (28%) recrudesced after initial involution, and 2 of 29 (7%) recurred completely, admitting the possibility that more lesions would recur over a longer follow-up interval. Furthermore, longer term studies would be required to answer this uncertainty.

In several lesions, clearing was associated with cutaneous depression, perhaps because of sudden involution of the enlarged sebaceous lobules. Multiple treatments using a lower fluence or single, rather than stacked, pulses may achieve the desired result without this complication. In fact, pulse stacking with the pulsed-dye laser may inflict nonspecific thermal injury to tissue preheated by immediately preceding pulses, beyond the selective photothermolysis of blood vessels. The erosion, crusting, and keratinocyte necrosis observed in several patients are evidence of this type of diffusion of thermal damage outside the chromophore-targeted structure.

Confocal imaging elucidates the vascular nature of sebaceous hyperplasia, visualizing the "crown" of blood vessels that surround the dilated sebaceous duct. Clearly, these lesions are amenable to selective targeting by the pulsed-dye laser. Indeed, confocal images taken after treatment reveal amorphous, refractile cords filling the shapes of the original vessels. These cords of agglutinated red blood cells seen after pulsed-dye laser treatment have been previously demonstrated by means of CM in a cherry angioma[15] and by means of conventional pathologic study of port-wine stains.[16-18]

Interestingly, the "crown" of vessels reappears in images taken 2, 4, and 8 weeks after treatment, without significant or reproducible differences from morphology before treatment. Whether involution of sebaceous hyperplasia is achieved through temporary ischemia or through thermal diffusion after pulse stacking remains unclear. Perhaps cellular growth inhibitors are released as a result of laser impact. However, our unpublished data, which suggest that sebaceous gland lipids do not absorb 585-nm light, would refute the possibility of a direct effect of pulsed-dye laser light on the gland itself. Although documenting a lack of permanent change in the sebaceous duct and its surrounding vasculature, in this study the CM was not able to image to the depth of the sebaceous gland lobules themselves, which clearly undergo a permanent decrease in size in all treated lesions.

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