Background: High-energy pulsed carbon dioxide (CO2) lasers have been used extensively to resurface wrinkled and photodamaged skin with a low risk of scarring. Results of histological studies demonstrate precise ablation depths in treated skin with minimal thermal damage to underlying tissue. Our objective was to determine if a pulsed CO2 laser could effectively ablate superficial malignant cutaneous neoplasms (superficial multifocal basal cell carcinoma [BCC] and squamous cell carcinoma [SCC] in situ).

Observations: Thirty superficial neoplasms (17 BCCs and 13 SCCs) and their surrounding 3-mm margins were treated with either 2 or 3 passes of a pulsed CO2 laser (500 mJ, 2-4 W) using a 3-mm collimated handpiece. The treated areas were subsequently excised and evaluated histologically by serial sectioning at 5-µm intervals for residual tumor at the deep and lateral margins. Average patient age was greater for those with SCCs than for those with BCCs (76.5 vs 56.7 years; P = .001). The average tumor thickness of SCC in situ was significantly greater than that of superficial BCC (0.57 vs 0.34 mm; P = .01). All (9 of 9 patients) BCCs were completely ablated with 3 passes, and residual tumor in the deep margins was seen in 5 of 8 patients treated with 2 passes of the pulsed CO2 laser (P = .005). Incomplete vaporization of the SCC depth was seen in 3 of 7 patients treated with 3 passes and in 2 of 6 patients treated with 2 passes. Those SCCs incompletely treated were significantly thicker than those completely ablated (0.65 vs 0.41 mm; P = .01). Positive lateral margins were seen in 1 BCC and 3 SCC specimens.

Conclusions: Pulsed CO2 laser treatment can be effective in ablating superficial BCC. Treatment of the neoplasm and a minimum of 4-mm margins with 3 passes (500 mJ, 2-4 W) is recommended for complete vaporization using this laser system. Because 3 passes did not completely ablate all SCC in situ, use of this modality alone is not recommended for treatment of thick or keratotic lesions. No direct comparison of efficacy can be made with other destructive modalities that have not been evaluated with comparably sensitive histological techniques. Further study is needed to establish any cosmetic advantage of pulsed CO2 lasers over other destructive modalities for treatment of superficial malignant neoplasms and long-term cure rates.

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Treatment of Superficial Basal Cell Carcinoma and Squamous Cell Carcinoma In Situ With a High-Energy Pulsed Carbon Dioxide Laser

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BASAL CELL CARCINOMA (BCC) is the most common skin cancer.1 Although nodular BCC is the most common subtype, superficial BCC accounts for 10% to 17% of all BCCs2,3 and up to 38% of BCCs in certain locations, such as the neck.7 Squamous cell carcinoma (SCC) is the second most common cutaneous neoplasm, with in situ carcinoma accounting for approximately 12%.8 Collectively, superficial BCC and SCC in situ represent a substantial percentage of malignant cutaneous neoplasms.

Superficial BCC is confined to or contiguous with the epidermis, and SCC in situ by definition does not invade the underlying dermis. Because of the lack of deeper invasion, these skin cancers are usually treated with a variety of destructive modalities, such as cryotherapy or electrodesiccation and curettage, that may yield cure rates for BCC of greater than 90%.9-15 Hypopigmentation or atrophic scarring are common sequelae of these modes of treatment because of nonspecific injury to surrounding healthy tissue. Other methods of treatment, such as surgery or radiotherapy, may also produce visible scarring. Chemical destruction with 5-fluorouracil may result in an excellent cosmetic outcome but initially may produce significant inflammation, resulting in decreased patient compliance with treatment.

Laser technology also has been applied to the realm of cutaneous oncology. Initially, continuous wave lasers such as argon and carbon dioxide (CO2) were used to treat premalignant conditions such as actinic cheilitis and to ablate malignant lesions such as Bowen disease16 and BCC.17,18 Potential advantages included better visualization in a bloodless plane, shortened healing time, and better cosmetic outcome compared with electrodesiccation and curettage.18 However, because of the potential for nonspecific thermal damage, continuous wave lasers also may produce atrophic or hypertrophic scarring.19,19
PATIENTS AND METHODS

An open study design was approved by the institutional review board of the University of Massachusetts Medical Center, Worcester. Patients with biopsy examination–proved superficial multifocal BCC or SCC in situ were first presented with treatment options. Patients who chose to have their lesions excised rather than treated by other modalities were invited to participate in the study. Patients who were in poor health precluding surgery, pregnant, or younger than 18 years were excluded from the study. Patients with lesions smaller than 0.5 cm or large lesions whose excision would result in disfigurement or functional compromise were also excluded. Inadequate initial biopsy specimens that precluded measurement of tumor depth were also grounds for exclusion. Each site was photographed and measured before treatment. Clinical borders were estimated by visual inspection and were marked with gentian violet. After informed consent was obtained, local anesthesia was administered and the malignant neoplasms and 3 mm of surrounding skin were first treated with either 2 or 3 passes of a PCO2 laser using a 3-mm collimated handpiece at 500 mJ, 2 to 4 W. Gauze soaked in saline solution was used to remove vaporized debris after each pass. Four large specimens were biopsied, and each half was treated with 2 or 3 passes, as above. The treated sites and 1-mm margins were then excised and submitted for histological evaluation.

Paraffin-embedded specimens were serially sectioned at 5 μm and were stained with hematoxylin and eosin. Slides were examined by a dermatopathologist (R.M.) unaware of treatment group for the presence of residual tumor and depth of thermal effect as demonstrated by the presence of coagulation necrosis. The depth of residual tumor beneath the ablated surface was measured. In addition, initial biopsy specimens were examined and the maximal depth of the malignant neoplasm was measured from the surface stratum corneum. The thickness of the stratum corneum keratin was also measured.

Using statistical software (SAS, SAS Institute Inc, Cary, NC), discrete variables were compared using χ² tests and continuous variables were analyzed using Student t tests.

The high-energy pulsed CO₂ (PCO₂) laser is 1 of many recent advances in laser technology. Delivery of high fluences with a short pulse duration allows for superficial vaporization of tissue and results in substantially less nonspecific thermal damage to surrounding tissue compared with continuous wave laser treatment. Pulsed CO₂ lasers are used primarily for aesthetic resurfacing procedures and have a low incidence of scarring (<1%) when used for this purpose.20-23 Results of histological studies demonstrate precise ablation depths using PCO₂ lasers.24-26 One study29 of healthy skin treated with a PCO₂ laser (Ultrapulse 5000, Coherent Laser Corp, Palo Alto, Calif; 450 J, 4 W, 3-mm spot) revealed ablation of the epidermis to 20 to 30 μm with 1 pass, to the superficial papillary dermis with the second pass, and to deeper levels of the papillary dermis with subsequent passes.

Although treatment efficacy should be the primary concern, cosmesis is always a consideration when choosing a method of treatment. Theoretically, superficial skin cancers confined to the papillary dermis or above could be completely ablated with a PCO₂ laser and could minimize the potential for scarring. Fitzpatrick and Goldman27 described treatment of an SCC in situ on the nose with 1 pass of the PCO₂ laser (250 mJ, 8 W) with an excellent cosmetic result and no recurrence at 5 months. Kilmer and Chotzen28 reported treating a series of patients with nodular and superficial BCCs with a combination of curettage and 1 or 2 passes of the PCO₂ laser (450 mJ, 5 W) with no histological evidence of residual tumor and no known recurrences. We sought to define the efficacy of this PCO₂ laser alone for the treatment of superficial BCC and SCC in situ and suggested treatment parameters.

RESULTS

Twenty-three patients had 32 sites treated. Two patients treated were later excluded from the study: 1 patient with BCC because the initial biopsy specimen was inadequate to assess depth and 1 patient with SCC in whom deeper cuts revealed focal dermal invasion. The remaining treatment group consisted of 30 specimens (17 BCCs and 13 SCCs). Fourteen superficial skin cancers were treated with 2 passes of the PCO₂ laser and 16 were treated with 3 passes. Patients with SCC were significantly older (P <.001) than patients with BCC (Table 1). The average age of patients with superficial BCCs was 56.7 years, and the average age of patients with SCC in situ was 76.5 years. Most BCCs and SCCs were located on the trunk, arms, or legs. Lesion size ranged from 0.6 to 2.2 cm (Table 1).

Evaluation of the initial diagnostic biopsy specimens revealed that the average depth of the superficial BCCs treated was 0.34 mm (range, 0.16-0.64 mm) (Table 1). Squamous cell carcinomas were significantly thicker (P = .01), with an average depth of 0.57 mm (range, 0.22-1.28 mm). Differences in stratum corneum thickness were significant. Although BCCs typically demonstrated a thin stratum corneum, that of SCCs was significantly thicker.

### Table 1. Clinical and Histological Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Basal Cell Carcinoma (n = 17)</th>
<th>Squamous Cell Carcinoma (n = 13)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average size, cm</td>
<td>1.12 ± 0.46</td>
<td>1.33 ± 0.51</td>
<td>.24</td>
</tr>
<tr>
<td>Length</td>
<td>0.93 ± 0.31</td>
<td>1.02 ± 0.38</td>
<td>.47</td>
</tr>
<tr>
<td>Site, No. (%)</td>
<td>Trunk 8 (47)</td>
<td>6 (46)</td>
<td>.50</td>
</tr>
<tr>
<td></td>
<td>Arms or legs 6 (35)</td>
<td>3 (23)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Head and neck 2 (12)</td>
<td>4 (31)</td>
<td></td>
</tr>
<tr>
<td>Average age, y</td>
<td>56.7 ± 13.3</td>
<td>76.6 ± 11.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Average total thickness, mm†</td>
<td>0.34 ± 0.11</td>
<td>0.57 ± 0.28</td>
<td>.01</td>
</tr>
<tr>
<td>Average keratin thickness, mm</td>
<td>0.05 ± 0.02</td>
<td>0.09 ± 0.06</td>
<td>.03</td>
</tr>
</tbody>
</table>

†Measured from surface of stratum corneum on initial biopsy specimen.

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Table 2. Presence of Tumor at Deep Margins

<table>
<thead>
<tr>
<th>No. of Passes</th>
<th>No. of Margins</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinomas</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>.005</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinomas</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>.73</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Examination of excised treated specimens revealed ablation of the epidermis, with underlying coagulation necrosis of collagen fibers extending from 0.10 to 0.28 mm beneath the surface (average, 0.16 mm). A rete ridge pattern was often preserved after 2 passes and absent after 3 passes. All BCCs were completely ablated with 3 passes of the CO2 laser, whereas some residual tumor was seen in the deep margins in 5 of 8 sites treated with 2 passes (Table 2). This difference in treatment efficacy was statistically significant (P = .005). Residual tumor was seen lateral to the treated area in 1 patient, and excisional margins were all negative for tumor. Of the SCCs, no significant difference in ablation was seen with 2 or 3 passes. Three of 7 and 2 of 6 specimens still revealed focal areas of residual tumor in the center of the specimen after 3 and 2 passes, respectively. Three treatment sites demonstrated positive lateral margins beyond the treatment site but negative excisional margins.

Each treated site with positive deep margins was reviewed, and the depth of residual tumor was compared with the depth of the initial biopsy specimen. Of the BCCs not completely ablated by 2 passes of the CO2 laser, 1 positive deep margin revealed only a solitary fragment of basaloid cells just beneath the level of ablation on one 5-µm section. The remainder of specimens with residual tumor revealed basaloid islands beneath the level of ablation at a depth greater than that of the initial biopsy specimen.

Examination of residual SCC revealed thick stratum corneum with underlying SCC in situ (1 patient), persistent abnormal hyperplastic epithelium (2 patients), or abnormal keratinocytes extending down follicular epithelium (2 patients) (Table 3). Two tumors were bisected, and both sides treated with 2 or 3 passes were still positive for residual tumor. Comparison of the treated sides revealed only slightly greater ablation after 3 passes. The average thickness of incompletely treated SCCs was significantly greater than that of completely vaporized lesions (0.65 vs 0.41 mm; P = .01) when outliers were omitted. One thick keratotic SCC that was completely ablated was removed from this specific analysis because a significant amount of keratin was thought to be removed by the initial biopsy procedure.

Our demographic data are consistent with existing literature (Table 1). Patients with SCC in situ tended to be older than those with superficial multifocal BCC, which likely reflects the role of long-term UV exposure in the former. Superficial BCCs were most commonly located on the trunk. As also noted by McCormack and colleagues, mean age was younger than that of patients with other types of BCC. In our study, SCCs were also located mainly on the trunk. Results of other studies show a predominance of Bowen disease on the head, neck, and hands. The size and location of both types of tumor was limited by the design of the study to lesions that could reasonably be excised after laser treatment without cosmetic or functional compromise. For this reason, large lesions of either type located on the face were excluded.

All patients tolerated the treatment protocol well and without complications. Figure 1 demonstrates the typical appearance of a BCC preoperatively and postoperatively. Figure 2 demonstrates the appearance of an SCC in situ and 3-mm margins treated with 3 passes of the CO2 laser. Erythema and pinpoint bleeding at the site of the skin cancer but not in the treated margins were seen after laser vaporization (Figure 1, bottom, and Figure 2, bottom).

Histological data revealed an important difference in the relative thickness of superficial BCCs and SCCs in situ. Basal cells tended to be thinner, with minimal surface stratum corneum (Table 1). Squamous cells in situ tended to be thicker, with a greater range of thickness of both stratum corneum and underlying abnormal epithelium. This observation has important treatment implications. Thus, one would expect superficial BCCs to be more effectively ablated by the CO2 laser or by any other destructive modality than SCCs in situ.

Histological evaluation of the successfully treated specimens revealed ablation to the papillary dermis or upper reticular dermis with 2 and 3 passes (Figure 3). Previous studies with the same laser system on healthy skin revealed an ablation of the epidermis to 20 to 30 µm with the first pass, to the superficial papillary dermis with the second pass, and to deeper levels of the papillary dermis with subsequent passes at 450 mJ. Another study of healthy skin yielded similar results using different output (250 mJ, 3-mm spot), with ablation of 30 to 50, 100 to 150, and 200 µm with 1, 2, and 3 passes, respectively. Residual thermal injury manifested by coagulation necrosis of collagen fibers is limited to depths of 20 to 70 µm beneath the level of ablation with the CO2 laser and to greater depths with...
other systems. In this study, a rete ridge pattern was often preserved in areas treated with 2 passes but not with 3 passes. An underlying zone of coagulation necrosis of variable thickness was observed in all specimens averaging 0.16 mm. The exact total depth of CO2 laser effect was difficult to assess accurately because we had no method to reliably measure “missing tissue” in large treated areas. All superficial BCCs were completely ablated with 3 passes of the PCO2 laser but not with 2 passes. Although this difference was statistically significant (P = .005), examination of specimens with residual tumor in the deep margins revealed some interesting observations. The average depth of incompletely ablated BCCs on initial biopsy examination (0.37 mm) was not significantly different from that of all BCCs. The residual tumor burden was always small and was only noted on 1 or 2 sections in all patients. It is likely that any residual tumor found during this study would have been overlooked with routine histological sectioning. One specimen revealed only a small solitary island of basaloid cells just beneath the level of ablation on a solitary 5-µm section. It is difficult to predict whether this would lead to a recurrence if not subsequently excised. The remainder of the positive specimens revealed larger islands of BCC below the level of ablation in the dermis, suggesting the presence of an isolated nodular component not sampled on initial biopsy examination (Figure 4). It is unlikely that this nodular component would have been eliminated by subsequent passes of the laser. Although superficial BCCs represented 14.8% of all BCCs in 1 study, mixed nodulo-superficial tumors accounted for only 1.9% of specimens.

Results of our study suggest that this number may be even greater and could account for some recurrences after destruction of superficial BCCs. Overall, there did not seem to be a significant difference in efficacy of treatment of SCC in situ when using 2 or 3 passes of the laser. Lesion thickness, however, was an important factor in predicting complete ablation. The SCCs that were not effectively ablated were significantly thicker than those that were ablated (0.65 vs 0.41 mm; P = .01). The average depth of residual tumor beneath the ablated surface was 0.41 mm. Examination of treated specimens with residual tumor revealed areas of incomplete ablation of a hyperplastic atypical epidermis (Figure 5, top), thick stratum corneum still intact with no ablation of underlying SCC (Figure 5, bottom), or residual atypia extending to follicular epithelium intact below the level of ablation. These observations highlight some important potential pitfalls in PCO2 laser treatment of SCC in situ. Stratum corneum of SCCs was significantly thicker than that of BCCs. This cornified layer is essentially dehydrated and may not be as amenable to vaporization. It is also likely that abnormal keratinizing squamous cells may contain less water, the target chromophore for the PCO2 laser, than healthy epithelium or BCC, hence, making it less easily ablated by this method.

A few treated specimens revealed incompletely treated tumor at the lateral margins of laser treatment but not at the excisional margins (1 BCC and 3 SCCs). This demonstrates that our protocol to treat 3 mm beyond clinically apparent tumor would not be adequate for all superficial
skin cancers. Current recommendations for excisional margins for primary nonmorphea-form BCC range from 2 to 5 mm.30-36 Wolf and Zitelli33 demonstrated subclinical extension that was sufficiently excised using 4-mm margins in 95% of BCCs smaller than 2 cm. No data specifically address subclinical extension in superficial BCC. Likewise, Broadland and Zitelli36 demonstrated that 4-mm margins were required to completely excise SCCs smaller than 2 cm in 95% of cases, although SCC in situ was not specifically evaluated. In our study, excisions were performed 1 mm beyond the 3-mm margin of treatment, and all excisional margins were negative, so a 4-mm margin of treatment beyond the lesion would have been sufficient for all skin cancers in our series. Larger BCCs and SCCs (> 2 cm) are likely to have a greater radius of subclinical extension,31,33,36 and greater treatment margins are recommended.

This study has obvious limitations. Because of the inclusion and exclusion criteria, our sample of superficial skin cancers may not be representative of all superficial BCCs or SCCs in situ likely to be treated in the average clinical setting. Patients most likely to benefit from this therapy over other modalities, ie, those with large skin cancers on the face where excision was not in the patient’s best interest for cosmetic or functional reasons, were deliberately excluded so that all specimens could be excised and examined histologically. It is unclear whether these larger skin cancers would respond in a manner similar to the smaller ones treated here. We are currently in the process of evaluating the efficacy of this laser treatment in patients with larger lesions not amenable to excision that would gain the most benefit from this treatment modality. Currently, at least 3 passes are recommended for large superficial BCCs, and the judgment of the clinician should dictate whether additional passes are necessary depending on the size and location of the lesion. Another limitation inherent in the study is the small sample size. If the sample size was expanded, we could conceivably find that there is no difference in efficacy between 2 and 3 passes when treating superficial BCCs with the PCO2 laser.

Figure 3. Results of histological examination (hematoxylin-eosin, original magnification ×10) of basal cell carcinoma successfully treated with 3 passes of the ultrapulsed carbon dioxide laser reveal the absence of tumor with complete ablation of the epidermis upper papillary dermis. Note the thin zone of coagulation necrosis beneath the level of ablation.

Figure 4. Residual basal cell carcinoma after treatment of 2 passes of the laser (hematoxylin-eosin, original magnification ×10). Note the isolated island of basaloid cells in the dermis beneath the level of ablation consistent with an occult nodular component. Epidermis and superficial tumor were completely vaporized.

Figure 5. Top, Residual squamous cell carcinoma in situ after vaporization with 2 passes of the laser (hematoxylin-eosin, original magnification ×10). Note the ablation of the surrounding epidermis. Bottom, Focal residual SCC in situ (as seen in Figure 2, top and bottom) after 3 passes of the laser (hematoxylin-eosin, original magnification ×10). Note the thick stratum corneum still intact preventing ablation of underlying abnormal epithelium.
The histological sectioning techniques used in this study, ie, serial sectioning of the entire specimen at 5 µm, allowed us to detect small areas of tumor that might not have been detected by conventional techniques. To our knowledge, this technique has not been applied to the examination of tissue treated by cryotherapy, electrodesiccation and curettage, or CO₂ laser in other studies. The fact that residual tumor was detected might lead the casual reader to conclude that the CO₂ laser is less effective than other destructive modalities, but, in fact, the histological techniques used were simply more sensitive. It is unclear whether the residual tumor detected in some specimens would have been sufficient to lead to clinical recurrence.

In conclusion, the CO₂ laser is a potentially favorable method of destruction of superficial BCC. Currently, we recommend the use of at least 3 passes on clinically visible tumor and at least 4 mm of surrounding healthy skin. Initial biopsy examination of the lesion to confirm a superficial growth pattern is also recommended. Occult foci of nodular BCC may not be completely treated and can theoretically result in recurrence. Currently, use of the CO₂ laser alone for the treatment of SCC in situ cannot be recommended for all lesions, especially those that are hyperplastic or hyperkeratotic or that have significant follicular extension. It is possible that a combined approach of curettage to remove the outer stratum corneum, debulk the lesion, and further define the tumor margins may result in more complete ablation. Graham" reported greater long-term efficacy of cryotherapy after curettage than for cryotherapy alone for cutaneous malignant neoplasms. Adams and Price" reported a 50% incidence of residual tumor treated with the continuous wave CO₂ laser alone, and Kilmer and Chotzen" reported no evidence of recurrent tumor after BCC treated with curettage and 1 or 2 passes of the CO₂ laser. Although good cosmetic results have been reported with this technique, it is unclear whether the cosmesis is truly superior to that obtained with cryotherapy or electrodesiccation and curettage. Theoretically, less scarring could be anticipated with use of the laser because of less nonspecific thermal damage to underlying tissue. Hypopigmentation and atrophic scarring have been observed, however, after treatment with curettage alone. Our preliminary results suggest that these adverse effects are more common when treating nonfacial sites with the CO₂ laser. Although treatment efficacy is the primary concern, further study is also needed to establish any cosmetic advantage of CO₂ lasers over other destructive modalities. A longitudinal study observing superficial skin cancers treated with the CO₂ laser alone or in combination with curettage for cosmetic outcome and therapeutic efficacy is currently under way.

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