Outcomes of Long-Pulsed 1064 nm Nd:YAG Laser Treatment of Basal Cell Carcinoma: A Retrospective Review

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Background and Objective: Recent prospective trials have supported treatment of nonfacial BCC with long-pulsed 1064 nm Nd:YAG laser based on short-term histologic clearance rates. Studies have yet to identify the long-term clinical clearance rates of this specific laser therapy for BCC.
Study Design/Material and Methods: This is a retrospective review of BCC treated with long-pulsed 1064 nm Nd:YAG laser, which have been clinically monitored for at least 6 months, to assess for recurrence and cosmetic outcomes of the treated area.
Results: 16 BCC lesions (11 subjects) treated with 1064 nm Nd:YAG laser were enrolled. Our analysis revealed 100% clearance rate in all subjects (16 of 16 BCC) treated with long-pulsed Nd:YAG laser based on mean follow-up of 9 months (range 6–15 months). Minimal scarring and no long-term adverse events were noted.
Conclusions: This study supports the use of 1064 nm Nd:YAG laser as a therapeutic modality for BCC based on the absence of clinical recurrence upon a mean follow-up of 9 months. As studies progress, we are beginning to observe a potential role for laser as an alternative to patients who refuse surgery, have multiple co-morbidities, or decline non-surgical therapies. Laser treatment with 1064 nm Nd:YAG is an evolving, promising story that we continue to investigate to optimize parameters. Lasers Surg. Med. 9999:1–6, 2018.

Key words: basal cell carcinoma; 1064 nm Nd:YAG; optical coherence tomography; laser therapy

INTRODUCTION

There has been growing interest in the spectrum of nonsurgical therapies available for basal cell carcinoma (BCC) that provide optimal cure rates and quality of life. This has led to several studies investigating lasers as an effective nonsurgical alternative. Because many of these investigations resulted in high rates of recurrence, necessitated multiple treatments, or lacked long-term data on recurrence rates, there has been insufficient evidence to recommend routine laser treatment of BCC [1–8].

An emerging alternative therapy, the 1064 nm Nd:YAG laser, has shown promising results for BCC treatment due to its depth of dermal penetration and affinity for tumor arterial network based on selective photothermolysis [9]. In 2015, a pilot study evaluated the utility of long-pulsed 1064 nm Nd:YAG laser treatment (Cynergy, Cynosure, Westford, MA) in 13 cases of BCC that were less than 1.5 cm in diameter, located on the trunk or extremities. Subjects were excluded if they were on anticoagulant therapy other than aspirin or non-steroidal anti-inflammatory drugs (NSAIDs). Treatments were administered with a 5 mm spot, fluence of 80 or 120 J/cm^2, and a pulse duration of 10 milliseconds (ms) with no epidermal cooling to the visible tumor and a 4 mm margin of adjacent skin. Standard excision was performed around 1 month after laser treatment for histologic evaluation of tumor response. This study demonstrated a 92% histologic clearance rate (12 of 13 BCC tumors) after one treatment, while 100% clearance rates were achieved when stratified to those treated with fluences of 120 J/cm^2 (10 of 10 BCC tumors). Treatments were tolerated without any significant adverse events [10].

This investigation led to a larger, prospective multicenter study by the same research team (AO, MA) evaluating the histologic clearance rates of long-pulsed 1064 nm Nd:YAG laser treatment in 33 subjects with BCC, who did not fulfill criteria for Mohs surgery [11]. Subjects

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: JA has no conflicts of interest. MA has stock options in Zalea, Inmode, Cytrellis, La Jolla Nanoparticle, serves on the Scientific Advisory board for Zeltiq Aesthetics, Soliton, Inc., Sciton Inc., and Sienna Biopharmaceuticals, and is a paid consultant for Merz and Alastin. AO is a member of the scientific advisory boards for Sciton, Merz, Inmode, Rodan and Fields, and Allergan, and is on the speakers bureau and receives honorarium from Sciton, Inmode, Alastin, and Allergan.

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were excluded if they were on anticoagulation therapy besides aspirin or NSAIDs at the time of study [11]. Similar to the open-label pilot study, subjects were treated with the 1064 nm Nd:YAG laser (Excel V, Cutera, Brisbane, CA) with parameters as follows: 5–6 mm spot, fluence 125 $-140\,J/cm^2$, pulse duration of 7–10 ms, 13–68 pulses, and no epidermal cooling. Treatments were tolerated with mild burning reported in several subjects during treatment. A month after treatment, subjects returned for standard surgical excision with a 5 mm clinical margin. The histologic clearance rate of BCC tumors after one session of laser treatment was 90.3% (28 of 31 BCC tumors). No significant adverse events were seen with laser treatment. Biopsy scars also improved after laser treatment, which was attributed to collagen remodeling from dermal heating. A significant limitation of this study is the lack of long-term evaluation as excisions were performed 30 days after laser treatment.

MATERIALS AND METHODS

This is an IRB-approved retrospective, multi-center study evaluating the efficacy and safety of the 1064 nm Nd:YAG laser for treatment of BCC. Data for this retrospective study were obtained from UC San Diego (UCSD) and Massachusetts General Hospital (MGH). Between April 2017 and July 2018, subjects who were treated with long-pulsed 1064 nm Nd:YAG laser for BCC were screened for the following inclusion criteria: (i) documented biopsy-proven diagnosis of BCC; (ii) treatment of BCC with 1064 nm Nd:YAG laser with specified parameters; (iii) minimum of one follow-up visit at least six months after laser treatment. Subjects without documentation of any signs indicating clinical recurrence of the treated area and those with previous treatments to BCC were specifically excluded.

Electronic outpatient records were reviewed using a standardized data extraction form. Demographic and tumor characteristics, laser parameters, adverse events, interval of follow-up, signs of clinical recurrence during follow-up visits, and quality of scar were recorded. If biopsy was required at the follow-up visit, pathology data from the biopsy was noted. AO and MA participated as the laser surgeons and assessed signs of clinical recurrence, which included evidence of ulceration or crusting, pain or tingling, papule/nodule near treated area, oozing, or bleeding [1,12].

RESULTS

Eleven subjects with sixteen cases of BCC (aged 31–85 years old) that were treated with the 1064 nm Nd:YAG laser were enrolled (Table 1). Ten out of 11 subjects had a past medical history of BCC in locations other than the treated laser site; eight subjects had been treated with Mohs surgery, electrodessication and curettage, and excision for their prior BCC. One subject had a history of Curry-Jones syndrome and preferred a laser surgical alternative after undergoing multiple traditional surgical treatments for BCC.

TABLE 1. Patient Demographics

	All BCC cases ($n = 16$)
Number of subjects	11
Gender (Female:Male)	1:3
Mean age in years	58.8 (range: 31–85)
Ethnicity	
Non-Hispanic Caucasian	15
Hispanic/Latino	1

Subtypes of BCC treated included superficial and nodular (Table 2). Of note, although one subject had four BCC fulfilling criteria for Mohs Micrographic Surgery [13] (3 within "H-zone," 1 within "M-zone"), the patient elected to proceed with laser treatment as he was a poor surgical candidate due to bleeding risk. Another patient whose two BCC were Mohs-appropriate ("M-zone") elected to proceed with laser treatment as he desired minimal downtime.

The average preoperative size was 6×6 mm and ranged from 4 to 21 mm. Including a 5 mm margin, BCC were treated with long-pulsed 1064 nm Nd:YAG laser (Excel V, Cutera, Brisbane, CA) with the following parameters: 5 mm spot, fluence $140\,J/cm^2$, pulse duration of 8 ms, 9–45 pulses. Pulses were delivered evenly throughout the tumor and the 5 mm margin. The treated area was allowed to cool before secondary passes were administered until the clinical endpoint was achieved. The number of pulses was tailored according to the clinical endpoint, which included greying and slight contraction (Fig. 1). The device was held approximately 2–3 mm above the skin's surface to avoid epidermal cooling from the sapphire window.

In all cases, 3 cc of 5 mg/ml lidocaine hydrochloride 0.5% was injected directly into the treated area prior to laser.

TABLE 2. BCC Characteristics

	All BCC cases ($n = 16$)
Location	
Head/Neck	6
Chest	3
Back	3
Upper extremities	2
Lower extremities	2
Subtype	
Superficial	3
Nodular	8
Superficial and Nodular	5
Preoperative size in mm (mean, range)	6×6, 4–21
Reason for Laser	
Concern about surgical downtime	10
Concern about cosmesis	2
Poor surgical candidates	4

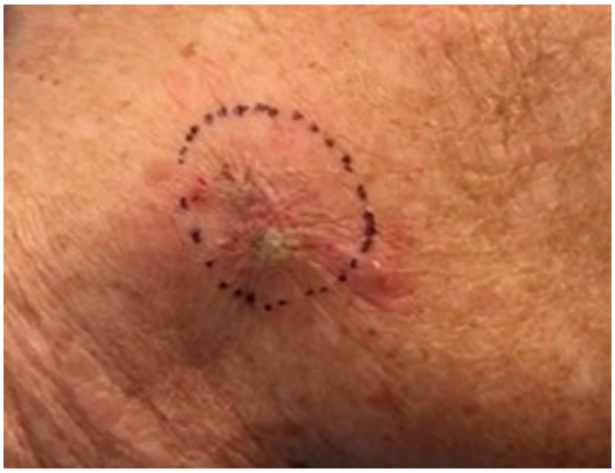

Fig. 1. Clinical endpoint of 1064 nm Nd:YAG laser therapy for BCC. Clinical endpoints with 1064 nm Nd:YAG laser treatment of BCC include graying and slight contraction as depicted in this photograph.

Epinephrine was not used because of its vasoconstrictive effect on our target tumor vasculature. Overall, treatments were tolerated. Immediate side effects of laser included mild purpura, edema, erythema, blistering, superficial erosion, and slight greying of tissue. Patients reported postoperative healing course of 2–3 weeks, which included redness, tenderness, and blistering, however this was not objectively evaluated.

All subjects (16 of 16 BCC) showed a complete clinical response to one session of the long-pulsed 1064 nm Nd:YAG laser treatment after a mean follow-up of 9 months (range: 6–15 months) (Fig. 2). Optical coherence tomography (OCT) was obtained of a BCC on the neck before and immediately after laser treatment (Fig. 3). Scarring was observed in three treated sites on the neck and back. Although one subject reported a history of keloidal formation after excision and electrodessication and curettage, no keloidal formation was noted at the laser-treated site after 12 months of clinical monitoring. No long-term adverse events were noted.

DISCUSSION

Larger diameter, friable telangiectatic vessels is a prototypic feature of BCC [5,11]. Delivering sufficient energy with a pulse duration shorter than the thermal relaxation time of tumor vasculature can cause irreversible vascular destruction leading to tumor regression. An added advantage of photothermal vascular targeting over conventional destructive or excisional treatments is the potential preservation of normal tissue surrounding the tumor, thereby reducing morbidity and optimizing cosmesis [10]. This selectivity, as supported by OCT imaging, is distinct from non-specific destruction by electrodessication or carbon dioxide laser. OCT allows for real-time assessment of the tumor based on the projection of infrared light onto the skin that causes light refraction of skin structures of varying optical properties [14]. Figure 3 demonstrates the immediate selective thermal damage on the tumor's vascular supply by the long-pulsed Nd:YAG laser, while conserving surrounding vasculature of normal tissue.

In this retrospective review, we have demonstrated that treatment with long-pulsed Nd:YAG laser revealed a 100% clearance rate in all subjects (16 of 16 BCC) based upon mean follow-up of 9 months (range 6–15 months). The rate of spontaneous clinical clearance for BCC after biopsy has been reported to be approximately 20% [15], thus our results cannot be explained by chance alone.

Prior histological studies have served as our platform to optimize parameters for this specific laser therapy for BCC. Based on the pilot study, we observed that clearance rates were higher in BCC treated with higher fluences. We also increased the margin size since previous tumors were positive due to inadequate margin control and not necessarily because of lack of laser efficacy [10,11]. In contrast to the pilot and expanded studies, all subjects were injected with lidocaine without epinephrine prior to the procedure to promote tolerability.

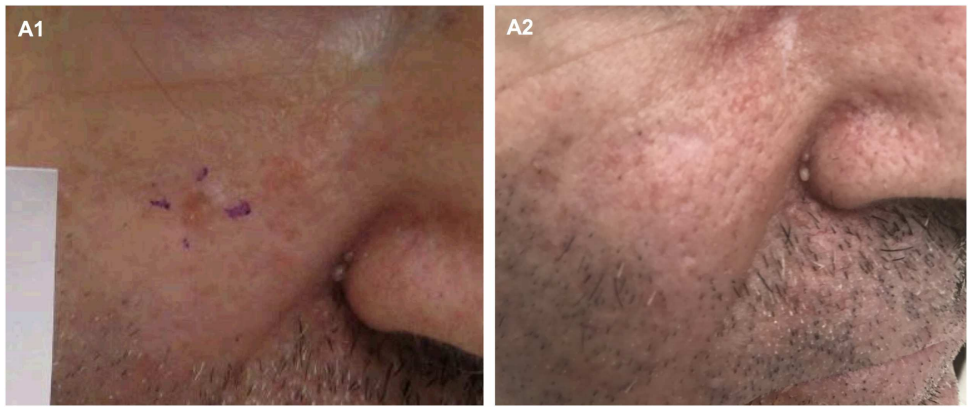

Fig. 2. Clinical Images of BCC before and after treatment with 1064 nm Nd:YAG laser therapy. A: Clinical images of BCC before (**A1**) and 10 months after (**A2**) laser treatment.

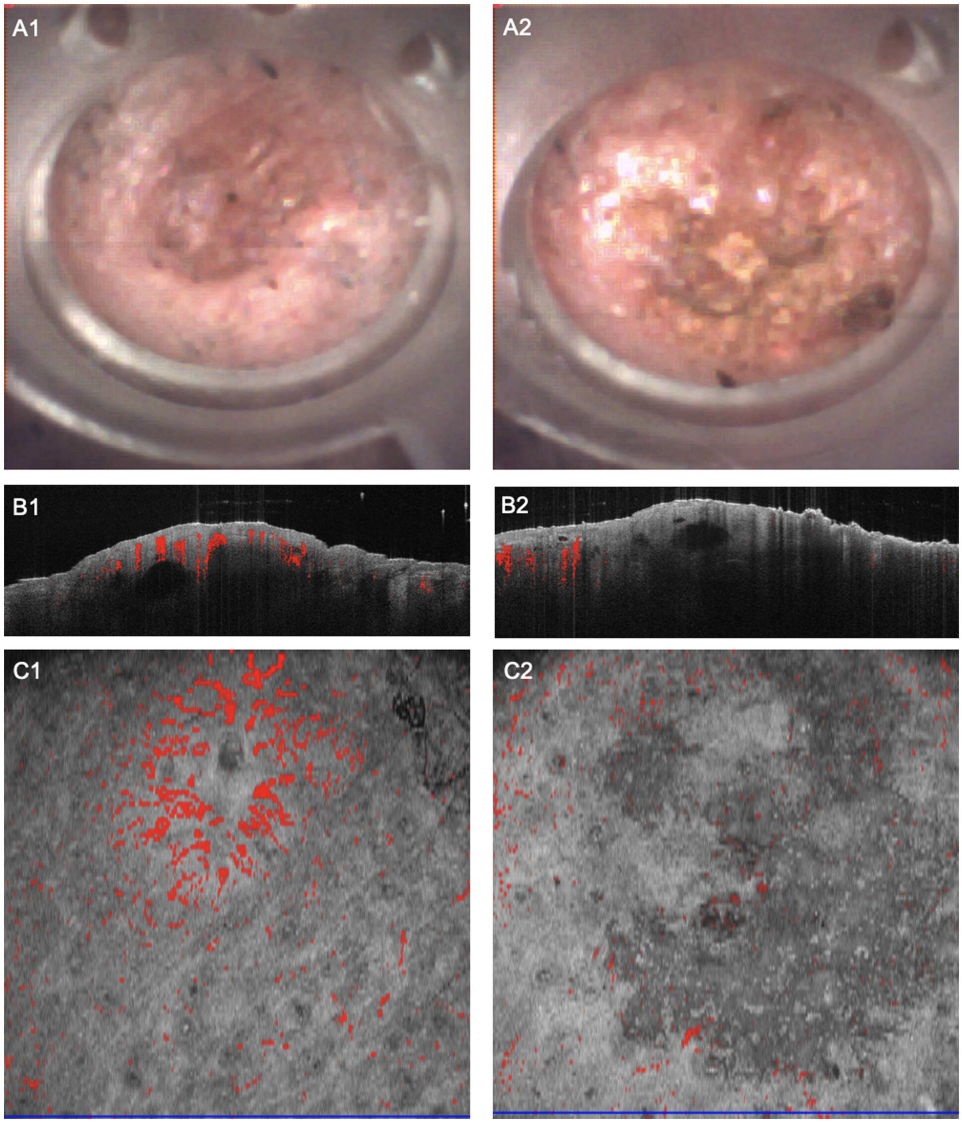

Fig. 3. Optical coherence tomography of BCC before and after laser treatment. **A**: Clinical images of BCC before (**A1**) and immediately after (**A2**) laser treatment; **B**: Structural views of BCC before (**B1**) and immediately after (**B2**) laser treatment; **C**: En face views at 150 micrometers depth of BCC before (**C1**) and immediately after (**C2**) laser treatment.

None of the subjects were on anticoagulants in the current study, except for NSAIDs. It has been suggested that by blocking the intravascular coagulation cascade, anticoagulants may hinder effective treatment of BCC with vascular selective lasers, such as the 1064 nm Nd: YAG [5,10,11]. Prospective trials are in progress to further assess the response of BCC to laser therapy in the setting of anticoagulation.

Our results are similar to those of a study using a continuous-wave 1064 nm Nd:YAG laser for BCC, which revealed a clearance rate of around 97% after 3–5 years of clinical monitoring; however, high rates of scar formation were seen as a result of the continuous rather than pulsed nature of energy delivered [16]. In our analysis, similar to the pilot and expanded studies, biopsy scars were noted to improve in some cases after laser treatment, likely secondary to collagen remodeling from dermal heating [10,11]. As noted in our results, some areas considered high risk for scar formation (back and neck) displayed minimal scarring after treatment, however, this was considered favorable over a surgical scar, and thus cosmetically acceptable to the patients.

Although we do not promote the use of laser to treat BCC that fulfill Mohs appropriate use criteria, our review included subjects treated with long-pulsed Nd: YAG laser for BCC that fulfilled criteria for Mohs surgery (6 of 16 BCC). These subjects had previously undergone Mohs surgery, and preferred a nonsurgical approach due to bleeding risk or exhaustion from multiple surgeries. To our knowledge, only one other

study evaluated the clinical efficacy of Nd:YAG treatment of facial BCC with reported recurrence rate of 3.1% at 13 months [17]. Pulse dye laser has also been investigated to treat facial BCC with reported clinical clearance rates of 75% at a mean follow-up of 11 months [18]. Infiltrative, nodular, or mixed subtypes of BCC were more likely to recur than others. Patients who are poor surgical candidates or who prefer an alternative to Mohs surgery may consider laser treatment as an alternative modality for their BCC.

In current literature, there are several studies evaluating recurrence rates of various nonsurgical approaches to BCC. For example, cryosurgery has reported recurrence rates ranging from 6.3% at 1 year to 39% after 2 years of follow-up [1,19–22]. Topical formulations, such as imiquimod and 5-fluorouracil, have reported clinical clearance rates of 60–80% over 3–12 months and 50–90% over 4 months, respectively [1,23,24]. While a head-to-head analysis has not been performed, long-pulsed 1064 nm Nd:YAG may be a preferred alternative when compared with other nonsurgical alternatives based on our clinical clearance rates.

This retrospective review supports our prior results that the 1064 nm Nd:YAG laser shows promise as a treatment alternative for BCC in poor surgical candidates or those who prefer nonsurgical management. The advantages of using pulsed, high-fluence 1064 nm Nd:YAG laser for BCC include minimal downtime, lack of significant adverse events, improved efficiency, cosmesis, and tolerability when combined with anesthesia [10,11]. Laser therapy decreases the potential for wound complications, such as infections (lack of open wound) and irritant or allergic contact dermatitis (does not involve use of bulky dressing). Additionally, patients are not required to return to the office for suture removal. These advantages are supported by the observation that a quarter of our subjects opted for laser therapy for other BCC after undergoing a single session of laser therapy. Of note, treatments were billed under malignant destruction depending on the size and location of the tumor.

Limitations of this study include sample size and the study's inherent retrospective nature. Since laser therapy on superficial and nodular BCC were investigated, the utility of laser treatment of aggressive subtypes (infiltrative, morpheaform) cannot be extrapolated based on the results of this study. Moreover, BCC in this study were small tumors, which limits generalizability to the larger variety in which laser treatment may be of particular interest. Lastly, a follow-up period of at least 5 years, which has been used for surgical trials, may further elucidate the potential for recurrence [1]. Although we cannot completely exclude a role of non-selective bulk heating as a result of the Nd:YAG laser, OCT imaging and relative lack of scar support the selectivity of this treatment.

The authors would like to emphasize that the 1064 nm Nd:YAG laser has a narrow therapeutic window as a consequence of longer pulse widths, higher fluences, and higher arterial absorption, and thus carries risks of scarring and ulceration. There is a risk of atrophic scarring especially when treating alar telangiectasias with this laser. This device should be used cautiously in the hands of an experienced laser surgeon.

CONCLUSION

Laser therapy with long-pulsed 1064 nm Nd:YAG shows promise for treating BCC based on the 100% clearance rate noted after a mean follow-up of 9 months. Minimal scars were observed, but were favorable over surgical scars. Our subjects opted for laser treatment because of minimal downtime, optimal cosmesis, or poor surgical candidacy. Prospective trials are in progress to establish the long-term clearance rates and cosmetic outcomes of BCC after treatment with 1064 nm Nd:YAG. Thus, laser treatment with 1064 nm Nd:YAG is an evolving, promising story that we continue to investigate to optimize parameters.

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