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CLINICAL REPORT

# Optical coherence tomography-guided Nd:YAG laser treatment and follow-up of basal cell carcinoma

**Stefanie Kranz MD[1] | Gisela Brunnmeier[1] | Pelinsu Yilmaz MD[1] | Janis Thamm[1] | Stefan Schiele MSc[2] | Gernot Müller MD[2] | Clara Key[1] | Julia Welzel MD[1] | Sandra Schuh MD, MSc, FEBDV[1]**

[1]Department of Dermatology and Allergology, Augsburg University Hospital, Augsburg, Germany

[2]Faculty of of Mathematics and Natural Sciences, Institute of Mathematics, University of Augsburg, Augsburg, Germany

**Correspondence**

Sandra Schuh, Department of Dermatology and Allergology, Augsburg University Hospital, Augsburg, Germany.
Email: sandra.schuh@uk-augsburg.de

## Abstract

**Objectives:** Basal cell carcinoma (BCC) is the most common skin tumor with an annually increasing incidence. Standard care requires several visits for diagnosis and treatment. Optical coherence tomography (OCT) as a diagnostic tool increases the sensitivity (95%) and specificity (77%) of the diagnosis of BCC. Although laser therapy is not the standard of care, the long-pulsed 1064 nm Nd:YAG laser seems to be a promising option. However, data are scarce. The published papers had a short follow-up (FU) time and used to some extent inferior methods to detect complete tumor clearance. To address this research gap, this study evaluates the efficiency of laser treatment by FU OCT. We pursue a patient-focused approach and combine OCT with Nd:YAG laser treatment in one procedure.

**Materials and Methods:** The study was conducted as a prospective, single-center trial that recruited biopsy-confirmed or OCT-proven BCC with a tumor thickness of less than 1.2 mm. Patients underwent two or three repeated sessions with the Nd:YAG laser (5–6 mm spot, fluence of 120–140 J/cm$^2$, pulse duration of 8–10 milliseconds). Each BCC was assessed at baseline, and 3 and 12 months after laser treatment by clinical image, dermoscopy, and OCT. Incomplete tumor clearance (ITC) was defined as a clearly detectable BCC on the OCT image or a biopsy-confirmed BCC in the treated area.

**Results:** Forty-five patients completed the 12-month FU (46.7% women; median age of 74.0 [52–88] years) with a total number of 78 BCC lesions. At baseline, all patients had their BCC diagnosed by OCT (tumor thickness of 0.6 [0.4; 0.8] mm), 15.4% lesions were additionally diagnosed by histopathology. The most common subtype of BCC was superficial (48.7%), followed by nodular (47.4%) and infiltrative (3.8%). ITC rate after the treatment using Nd:YAG laser was 30.8% (95% CI: 20.8%–42.2%) (24/78) after 3 months and 7.4% (95% CI: 2.1%–17.9%) (4/54) after 12 months. ITC was not associated with histological subtype, tumor thickness, or location. If ITC was detected, the lesion was treated again. Out of 19 lesions with at least one additional laser treatment, 7 lesions (36.8%) suffered from incomplete tumor removal. In 46.7% of the treated lesions, the cosmetic outcome was rated as moderate or severe scarring after 12 months.

**Conclusion:** Our results demonstrate that the ITC rate of BCC treated with the Nd:YAG laser is much higher (up to one-third) than reported, although the laser settings were identical to prior studies. This is especially evident at the 3-month

FU. In addition, we witnessed a larger number of side effects and a worse cosmetic outcome compared to previous studies.

**KEYWORDS**

basal cell carcinoma, long-pulsed 1064 nm Nd:YAG laser, optical coherence tomography, treatment of basal cell carcinoma

## INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin tumor with an annually increasing incidence[1,2] and a lifetime risk of more than 10%.[3] Even though BCC is rarely life-threatening due to metastasis, the malignant potential of BCC lies in its nature to grow locally invasive and destructive and, therefore, may cause substantial functional and cosmetic morbidity.[4–6] In many cases, several consultation hours at a specialist are required in the process of diagnosis and therapy adjustment of BCC. The laborious and time-consuming process for the patient upon implementation of adequate therapy, moreover, may be associated with a significant financial burden for the healthcare system. Hence, BCC is considered a serious and complex public health problem, calling for substantive approaches and improvements, in terms of diagnostics as well as for expanding the spectrum of adequate treatment modalities.[7]

Currently, the decisions making for either a surgical or conservative (radiation, photodynamic therapy, cryotherapy, imiquimod, and 5-fluorouracil) therapy approach in the treatment of BCC, depends on the individual risk of incomplete tumor clearance (ITC).[8] Surgical excision is the most commonly used therapy, but it is usually costly and may cause unwanted side effects, such as bleeding, infection, scarring and cosmetic dissatisfaction.[9] In addition, excision of BCC without the use of margin-control is associated with an ITC rate of up to 24%.[8] Similarly, the use of topical agents in superficial BCC requires strict patient adherence for several weeks and often results in ITC upon inadequate treatment,[10] especially in the nodular subtype.[2,11] Moreover, the subtype is of great importance as there are many mixed subtypes. It needs to be mentioned that for aggressive subtypes laser therapy may not be the ideal treatment. Laser therapy, which is oriented toward unclear clinical endpoints can also lead to poor cosmetic outcome, an overtreatment with scars or incomplete clearance.

The previously mentioned limitations of surgical and conservative treatment methods have recently led to the discovery of laser treatment as a potentially effective nonsurgical alternative.[4,5,12,13] Since tumor vessels in BCC, are reported to have a significantly larger diameter and to be more fragile than the vasculature in normal skin, the microvascular architecture appears to be the ideal target to impair the tumor tissue at a critical point, while the epidermis is spared.[4,14] While studies on repeated treatments using 585 and 595-nm pulsed dye laser (PDL) demonstrate inconsistent results,[15] the 1.064-nm long-pulsed Nd:YAG laser may provide the most promising approach for laser-treatment of BCC, which is currently not standard of care. Unlike the PDL, the Nd:YAG laser achieves deeper penetration in the dermis, resulting in a better outcome.[5,16] However, previously conducted prospective studies on Nd:YAG laser in BCC did not only cover a low number of treated BCC (a maximum of 31), but also exhibited several limitations (e.g., certain locations, patients with anticoagulation were excluded, short FU time and show to some extent inferior methods to detect complete tumor clearance).[5,13,17]

In recent years, emerging, noninvasive imaging techniques, such as optical coherence tomography (OCT), were introduced to the clinical setting to aid and guide the clinical and dermatoscopic examination in the diagnosis of BCC. The device increases the sensitivity (95%) and specificity (77%) in the detection of BCC compared to clinical and dermatoscopic diagnoses alone.[18] These key features of OCT imaging may reduce the need for invasive skin biopsy significantly as Adan et. al have shown recently.[19,20] Because of the high negative predictive value (92.1%) of OCT in diagnosis of BCC, OCT can also be used to monitor therapy response and to detect ITC of BCC, eventually.[19,21] Since the highest risk of recurrence of treated BCC is reported to happen within 1–4 years after therapy, OCT may resemble a pivotal tool to surveille and guide long-term follow-up (FU) of BCC.[22]

In this study, an innovative, patient-focused approach was implemented, using OCT imaging as a diagnostic tool, and delivering laser treatment to BCC lesions within the same consultation. OCT was used to increase the period of FU and to facilitate the detection of ITC as well as the assessment of the cosmetic outcome. In this study, we hypothesized that OCT-guided Nd:YAG laser treatment may be an efficient and safe tool in the treatment of BCC.

## MATERIALS AND METHODS

To investigate the hypothesis of this study, a prospective, single-center study design was chosen and carried out at the Department of Dermatology and Allergology, University Hospital Augsburg, approved by the ethical committee of the LMU Munich (Protocol Number 18-718). Between 2018 and 2022, adult patients (18 years of age, or older) with OCT-proven or biopsy-confirmed diagnosis of BCC and a tumor thickness of less than 1.2 mm were recruited. Up to three BCC lesions were considered per patient. Each

individual included, received detailed information on the planned treatment, treatment alternatives, and possible adverse effects and complications. In addition, written informed consent was obtained from all patients before enrollment. Patients' data were anonymized to comply with data and privacy regulations.

Data collected from every single individual included age at baseline, sex, immunosuppression, and anticoagulation. For each BCC lesion, tumor subtype (superficial (sBCC), nodular (nBCC), or infiltrative (iBCC), thickness, tumor diameter (> or <10 mm), and location were annotated. No size restrictions in terms of tumor diameter were applied; however, initial tumor thickness was not allowed to exceed a vertical maximum expansion of 1.2 mm. In addition, recurrent BCCs and BCCs, assigned to a surgical therapy (e.g., iBCC in the H-zone of the face), were excluded.

Each BCC was assessed at baseline, and at 3- and 12-month FU after laser treatment by clinical image (iPhone 12 Pro Camera; Apple Inc.), dermoscopy (ILLUCO IDS-1100; DermoScan GmbH), and OCT imaging (VivoSight Dx®; Michelson diagnostics Ltd.). In cases where no histopathology was available, OCT imaging was performed before the treatment to confirm diagnosis. In all cases, OCT was performed after treatment to detect ITC, as FU. ITC was defined as either appearance of distinct and definite BCC structures and morphology on OCT images or as a histologically proven BCC occurring in the treated area. OCT images were screened for typical BCC morphology.[23] Outcomes were classified at 3 and 12 months after laser treatment depending on ITC. When ITC was detected during FU, alternative therapeutical options (surgical excision, topical therapy, or retreatment with laser) were discussed with the patient. As a result, some patients with ITC received several laser treatments.

Each single laser treatment consisted of two to three repeated sessions (separated by a 3-minutes interval) using a long-pulsed 1064 nm Nd:YAG laser (Sciton Inc. and Candela Corp.). Similar to the published studies with Nd:YAG laser, a 5–6 mm spot, fluence of 120–140 J/cm$^2$ and a pulse duration of 8–10 milliseconds were used.[12,13,17] We clinically applied a 0.5 cm treatment margin to the lesion; OCT-mapping before therapy was not performed. Neither local anesthesia nor epidermal cooling was applied to avoid any negative effect on the vasculature.

After laser treatment, individuals were asked to classify experienced levels of pain on the visual analog scale (VAS) from 0 to 10. Occurrence of infection after treatment was documented. A 4-point scale (0 absent, 1 mild, 2 moderate, 3 severe) was used to assess scarring after 12 months. In addition, patient satisfaction was surveyed at the end of the study.

Patient characteristics were summarized by descriptive statistics. Continuous variables were tested with Shapiro–Wilk test for normality and described by median and quartiles or ranges. Categorical variables were expressed as counts and percentages. We computed 95% confidence intervals for recurrency rates using Clopper–Pearson exact method. We calculated Kaplan–Meier curves and confidence intervals using Greenwood's formula. A univariable generalized estimating equation (GEE) regression was fitted for each parameter to examine an association with ITC at 3 and within 12 months. For the comparison between satisfied and nonsatisfied patients, we used a Wilcoxon rank-sum test for continuous variables and a $\chi^2$ test or Fisher exact test for categorical variables. All statistical analysis was performed with R 4.1.1. and a $p < 0.05$ was considered statistically significant.

# RESULTS

## Patient and lesion characteristics

Initially, a total of 46 individuals was enrolled. A single individual dropped out due to unrelated health issues, leading to a final cohort of 45 patients (21 female, 24 male) and a total of 78 BCC lesions. The median age was 74.0 (range 52–88 years) years at baseline. Immunosuppression was present in 5/45 (11.1%) (with 9 BCC), anticoagulation in 16/45 (35.6%) (with 25 BCC) (Table 1). Most patients (39/45, 86.7%) adhered to the monitoring protocol.

**TABLE 1** Characteristics of patients ($n = 45$) and lesions ($n = 78$).

| | Patients | | Lesions | |
|---|---|---|---|---|
| | *n* | % | *n* | % |
| **Incomplete tumor clearance** | | | | |
| Incomplete tumor clearance at 3 months | 17 | 37.8 | 24 | 30.8 |
| **Patient characteristics** | | | | |
| Age, median (Q1, Q3) | 74.0 (65.0, 78.0) | | 74.0 (70.0–77.0) | |
| Sex | | | | |
| Male | 24 | 53.3 | 46 | 59.0 |
| Female | 21 | 46.7 | 32 | 41.0 |

(Continues)

**TABLE 1** (Continued)

| | Patients | | Lesions | |
|---|---|---|---|---|
| | *n* | % | *n* | % |
| Immunosuppression | 5 | 11.1 | 9 | 11.5 |
| Anticoagulation | 16 | 35.6 | 25 | 32.1 |
| **Lesions characteristics** | | | | |
| Number of lesions | | | | |
| 1 | 23 | 51.1 | | |
| 2 | 8 | 17.8 | | |
| 3 | 14 | 31.1 | | |
| Subtype | | | | |
| nBCC | | | 37 | 47.4 |
| iBCC | | | 3 | 3.8 |
| sBCC | | | 38 | 48.7 |
| Location | | | | |
| Trunk | | | 38 | 48.7 |
| Extremity | | | 22 | 28.2 |
| Face | | | 18 | 23.1 |
| Tumor thickness (OCT), median (Q1, Q3) | | | 0.6 (0.4, 0.8) | |
| Tumor diameter (mm) | | | | |
| <10 | | | 41 | 52.6 |
| >10 | | | 37 | 47.4 |
| **Side effects** | | | | |
| Pain during treatment, median (Q1, Q3) | 6.0 (4.0, 7.0) | | | |
| Infection | 5 | 11.1 | | |
| **Treatment outcome** | | | | |
| Scarring[a] | | | | |
| Absent | | | 10 | 14.1 |
| Mild | | | 22 | 31.0 |
| Moderate | | | 19 | 26.8 |
| Severe | | | 2 | 2.8 |
| Satisfied with treatment | 35 | 77.8 | | |

Abbreviations: BCC, basal cell carcinoma; iBCC, infiltrative BCC; nBCC, nodular BCC; OCT, optical coherence tomography; sBCC, superficial BCC.

[a]Only lesions with a completed treatment.

All 78 BCCs were diagnosed using OCT (Table 2). In 12/78 (15.4%) lesions, additional biopsy was used to confirm diagnosis (Table 2). The most prevalent subtype was sBCC (38/78; 48.7%) followed by nBCC (37/78; 47.4%) and iBCC (3/78; 3.8%) with a median baseline tumor thickness of 0.35 mm (range: 0.14–0.72 mm) for sBCC, 0.83 mm (range: 0.50–1.57 mm) for nBCC and 0.68 mm (range: 0.43–1.00 mm) for iBCC on OCT imaging. Most BCCs were located on the trunk (38/78; 48.7%), on the extremities (22/78; 28.2%), rarely, in the

**TABLE 2** BCC subtypes diagnosed with OCT versus biopsy at first diagnosis.

| | Histology at first diagnosis (%) | OCT at first diagnosis (%) |
|---|---|---|
| nBCC | 8.1 | 91.9 |
| iBCC | 33.3 | 66.7 |
| sBCC | 21.1 | 78.9 |

Abbreviations: BCC, basal cell carcinoma; iBCC, infiltrative BCC; nBCC, nodular BCC; OCT, optical coherence tomography; sBCC, superficial BCC.

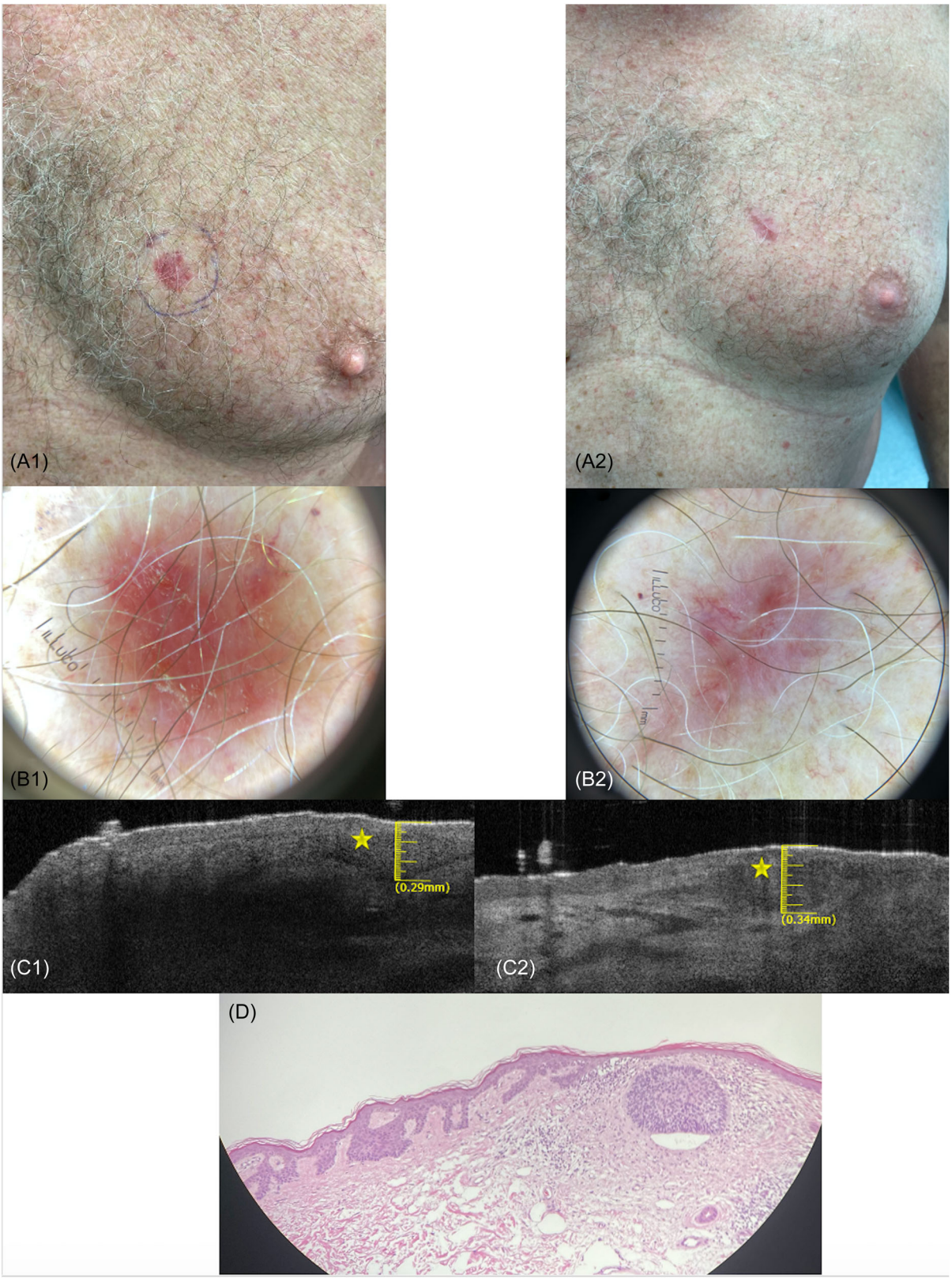


**FIGURE 1** Typical images of an incomplete tumor clearance of a basal cell carcinoma in a 63-year-old male patient localized at the sternum at baseline and at the 3-month FU; (A) clinic (iPhone 12 Pro Camera; [Apple Inc.]) at baseline (A1) and at 3-month FU (A2); (B) dermoscopy (ILLUCO IDS-1100; [DermoScan GmbH]) at baseline (B1) and at 3-month FU (B2); (C) optical coherence tomography (VivoSight Dx®, Michelson Diagnostics Ltd., Maidstone, image size: $6 \times 1\ mm^2$, lateral and axial resolution: $7.5\ \mu m \times 10\ \mu m$) with typical characteristics of a superficial basal cell carcinoma at baseline (C1) and at 3-month FU (C2); (D) histopathology at 3-month FU. FU, follow-up.

face (18/78; 23.1%). 37/78 (47.4%) BCCs had a tumor diameter >10 mm, especially on the trunk (65.8%) (Table 1). Three patients had a BCC larger than 1.2 mm but gave written consent and wanted to have laser therapy instead of surgery.

## ITC

At 3 months FU, 24/78 (30.8%, 95% CI: 20.8%–42.2%) of the lesions with a single laser treatment showed ITC on OCT. An example of ITC, comprising clinical images, dermoscopy, OCT, and histology at 3-month FU is given in Figure 1. In cases with complete tumor clearance at 3-month FU (54/78, 69.2%, see Figure 2), ITC was observed in 4 (4/54, 7.4%, 95% CI: 2.1%–17.9%) lesions at 12-month FU. 10 of 28 (35.7%) ITCs were diagnosed by biopsy in addition to OCT.

The ITC rates at 3-month FU (vs. complete tumor clearance) did not differ significantly between histological subtype (sBCC vs. nBCC vs. iBCC: 26.3% vs. 32.4% vs. 66.7% $p = 0.328$) and were not associated with the OCT-measured thickness ($p = 0.412$) (Table 3).

Overall, complete tumor clearance was reported in 50/78 (64.1%, 95% CI: 52.4%–74.7%) lesions. In detail, 9/18 facial (50.0%) and 41/60 (68.3%) nonfacial BCCs showed complete tumor clearance at 12-month FU (Figure 3), translating into no significant difference between the different locations ($p = 0.387$) as well as the tumor diameter ($p = 0.571$). ITC were found primarily in the marginal area of the lesions. Patients with ITC had similar characteristics (age ($p = 0.303$), immunosuppression ($p = 0.906$), and anticoagulation ($p = 0.545$) to those with tumor clearance (Table 3).

In the group of lesions with ITC after 3- or 12-month FU, 3/28 (10.7%) were treated with surgical excision, 5 with topical agents, and 19 with at least one further laser treatment. In one case, no further treatment was implemented at patient's request. 11/19 lesions with ITC required another treatment with laser and 8/19 lesions required two additional retreatments (median time between first and second treatment: 138 days; median time between second and third treatment: 217 days). Although the laser treatment was repeated, complete tumor removal could not be achieved in 7 (36.8%) lesions. In those cases, surgical excision was performed afterward. Of the seven lesions that could not be treated sufficiently by laser, two were sBCC, and five were nBCC. Only one of the BCC larger than 1.2 mm was among this group, the other two were treated successfully.

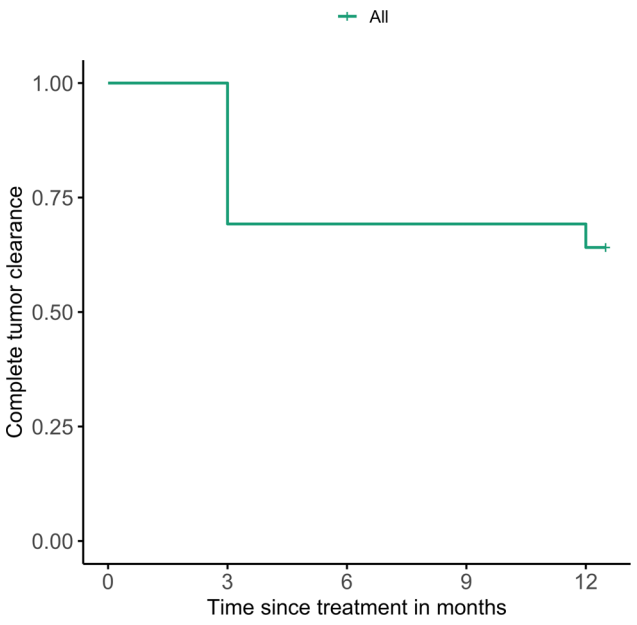


**FIGURE 2** Kaplan–Meier curve to visualize the proportion of complete tumor clearance. According to Greenwood's formula the proportion of complete tumor clearance was 69.2% (59.0%–79.5%) at 3 months and 64.1% (53.5%–74.7%) at 12 months.

## Side effects

Patients rated the pain during the laser treatment with six (median, quartile 4.0;7.0) on the VAS and described a burning sensation. One individual refused further laser treatments of other BCCs due to pain. Immediate side effects observed were edema, erythema, purpura, and blistering. Local infection occurred in 5/45 (11.1%) lesions, whereas systemic infection was not observed within the study population. In the group of cleared lesions treated with a single laser procedure, scarring was rated as moderate or severe on the 4-point scale in 21 (46.7%) lesions after 12 months (Figure 4). Thus, scarring was not uncommon after laser treatment. The tumor subtype ($p = 0.551$), thickness ($p = 0.216$), location ($p = 0.291$) had no impact on the cosmetic outcome. A diameter ≤10 mm had a higher fraction of positive cosmetic outcome than lesions with a diameter >10 mm (76.9% vs. 44.4%).

35/45 (77.8%) individuals stated that they would prefer laser treatment over other therapeutical options. The decision was not associated with tumor clearance after 12 months ($p = 0.281$), the best cosmetic outcome of a patient ($p = 0.559$) nor the worst cosmetic outcome ($p = 0.639$). There was a slight, but not significant, trend for a higher pain indication when patients were not satisfied with the

**TABLE 3** Comparison of lesions with and without incomplete tumor clearance at 3 months and within 12 months.

| | Incomplete tumor clearance at 3 months | | | Incomplete tumor clearance within 12 months | | |
|---|---|---|---|---|---|---|
| | Yes ($n = 24$), $n$ (%) | No ($n = 54$), $n$ (%) | $p$ Value | Yes ($n = 28$), $n$ (%) | No ($n = 50$), $n$ (%) | $p$ Value |
| **Patient characteristics** | | | | | | |
| Age of patient, median (Q1, Q3) | 75.5 (70.0, 78.0) | 73.0 (70.0–77.0) | 0.592[a] | 75.5 (72.2, 78.0) | 72.5 (70.0, 77.0) | 0.303[a] |
| Sex of patient | | | 0.171[a] | | | 0.171[a] |
| Male | 10 (21.7) | 36 (78.3) | | 12 (26.1) | 34 (73.9) | |
| Female | 14 (43.8) | 18 (56.2) | | 16 (50.0) | 16 (50.0) | |
| Immunosuppression | | | 0.753[a] | | | 0.906[a] |
| No | 21 (30.4) | 48 (69.6) | | 25 (36.2) | 44 (63.8) | |
| Yes | 3 (33.3) | 6 (66.7) | | 3 (33.3) | 6 (66.7) | |
| Anticoagulation | | | 0.842[a] | | | 0.545[a] |
| No | 17 (32.1) | 36 (67.9) | | 21 (39.6) | 32 (60.4) | |
| Yes | 7 (28.0) | 18 (72.0) | | 7 (28.0) | 18 (72.0) | |
| **Lesions characteristics** | | | | | | |
| Subtyp | | | 0.328[a] | | | 0.376[a] |
| nBCC | 12 (32.4) | 25 (67.6) | | 15 (40.5) | 22 (59.5) | |
| iBCC | 2 (66.7) | 1 (33.3) | | 2 (66.7) | 1 (33.3) | |
| sBCC | 10 (26.3) | 28 (73.7) | | 11 (28.9) | 27 (71.1) | |
| Location | | | 0.365[a] | | | 0.387[a] |
| Trunk | 8 (21.1) | 30 (78.9) | | 10 (26.3) | 28 (73.7) | |
| Extremity | 8 (36.4) | 14 (63.6) | | 9 (40.9) | 13 (59.1) | |
| Face | 8 (44.4) | 10 (55.6) | | 9 (50.0) | 9 (50.0) | |
| Tumor thickness (OCT), median (Q1, Q3) | 0.7 (0.4; 0.9) | 0.5 (0.4; 0.8) | 0.412[a] | 0.7 (0.4; 1.0) | 0.5 (0.4; 0.8) | 0.290[a] |
| Tumor diameter (mm) | | | 0.542[a] | | | 0.571[a] |
| <10 | 14 (34.1) | 27 (65.9) | | 16 (39.0) | 25 (61.0) | |
| >10 | 10 (27.0) | 27 (73.0) | | 12 (32.4) | 25 (67.6) | |

Abbreviations: BCC, basal cell carcinoma; iBCC, infiltrative BCC; nBCC, nodular BCC, OCT, optical coherence tomography; sBCC, superficial BCC.
[a]Results of the GEE analysis.

treatment (median [quartile] 7.0 [4.5, 9.8] vs. 6.0 [4.0, 7.0]; $p = 0.144$) (Table 4).

## DISCUSSION

In comparison to the currently available literature, this prospective study comprised and analyzed one of the largest sample size of BCCs treated with long-pulsed Nd:YAG laser.[4,5,13] We noticed a significantly higher rate of ITC after Nd:YAG laser treatment than reported in previous studies,[4,5,13,24] especially at 3-month FU. Only one study showed a similar high ITC rate of 29.6% at 2-month FU after a single laser treatment.[12]

Several factors were identified and may be responsible for the high ITC rate: First, the ITC detected were mainly in the marginal area of the lesions, suggesting that the laser distance to healthy skin was too narrow.

Second, whereas most other studies only used histopathology to diagnose ITC,[4,5,13] in this study, ITC was predominantly detected, using OCT. OCT for noninvasive treatment monitoring is essential as these patients want to avoid surgical procedures in the first place: Most of our patients preferred OCT over punch biopsy as diagnostic strategy for BCC, which aligns with the study by Adan et al.[19,25] OCT may not be able to distinguish between tumor remnants which are being degraded or actual active tumor cells. This assumption may explain why OCT-based detection of ITC is prone to

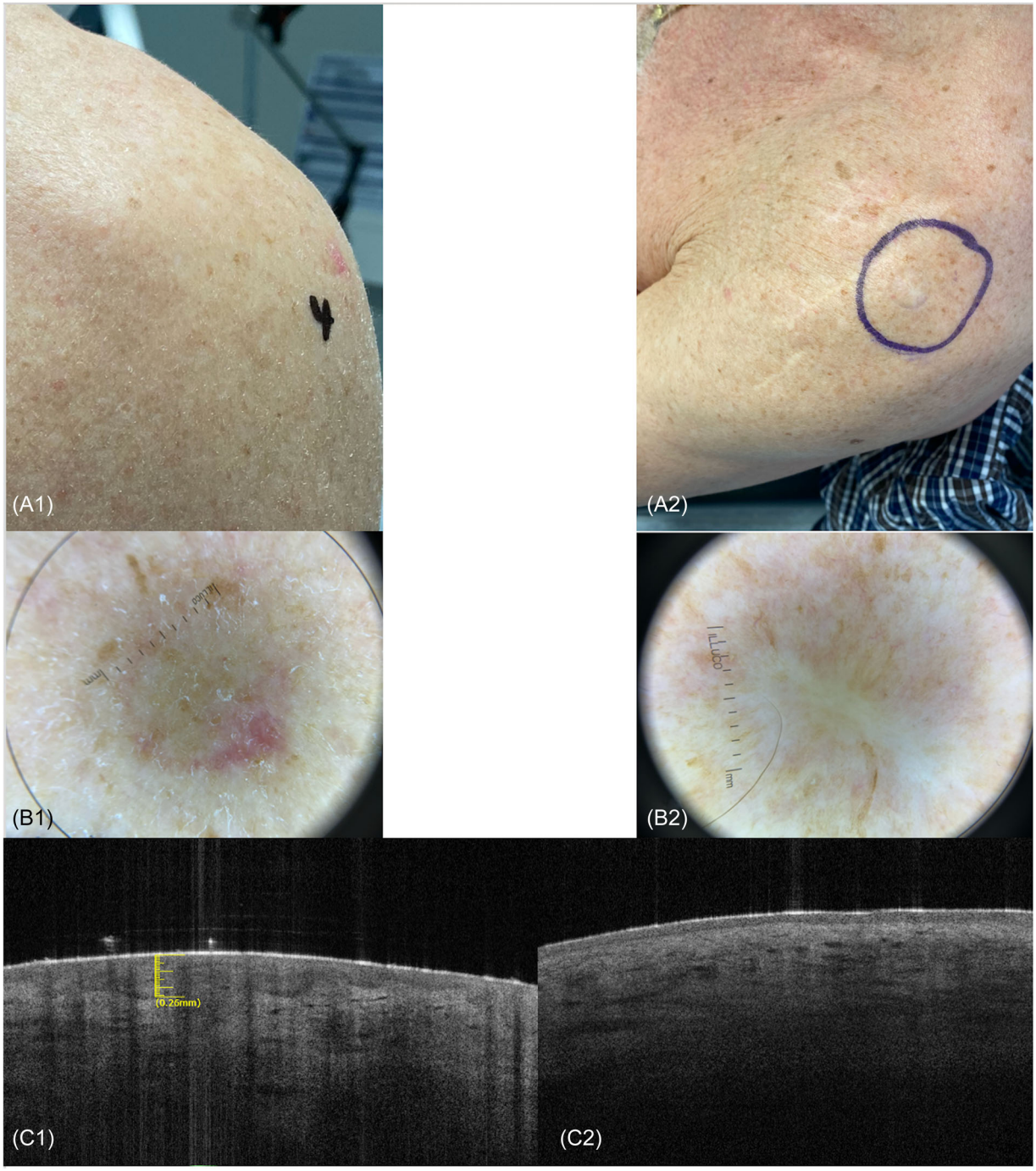


**FIGURE 3** Typical images of a complete tumor clearance in a 72-year-old male patient localized at the right upper arm at baseline and at the 12 month FU; (A) clinic (iPhone 12 Pro Camera; [Apple Inc.]) at baseline (A1) and at 12 month FU (A2); (B) dermoscopy (ILLUCO IDS-1100; [DermoScan GmbH]) at baseline (B1) and at 12 month FU (B2); (C) optical coherence tomography (VivoSight Dx®, Michelson Diagnostics Ltd., image size: $6 \times 1\ mm^2$, lateral and axial resolution: $7.5\ \mu m \times 10\ \mu m$) of a superficial basal cell carcinoma at baseline with a tumor thickness of 0.26 mm (C1) and fibrosis with complete tumor clearance at 12 month FU (C2). FU, follow-up.

more false positive results in the FU-period of laser treated BCC. Therefore, comparing the clearance rate using OCT versus the studies confirming the clearance rate on pathology is difficult. On the other hand, detection of BCC ITC using OCT might be even more accurate than punch biopsy: Adan et al. demonstrated that OCT-guided diagnosis of BCC is equal to punch biopsy.[19] In contrast to punch biopsy, which only allows a partly examination of a lesion, the great advantage of OCT is that it is possible to examine the entire lesion. Thus, even ITC in marginal areas can be detected. This fact is congruent with our observation, that ITC of BCC

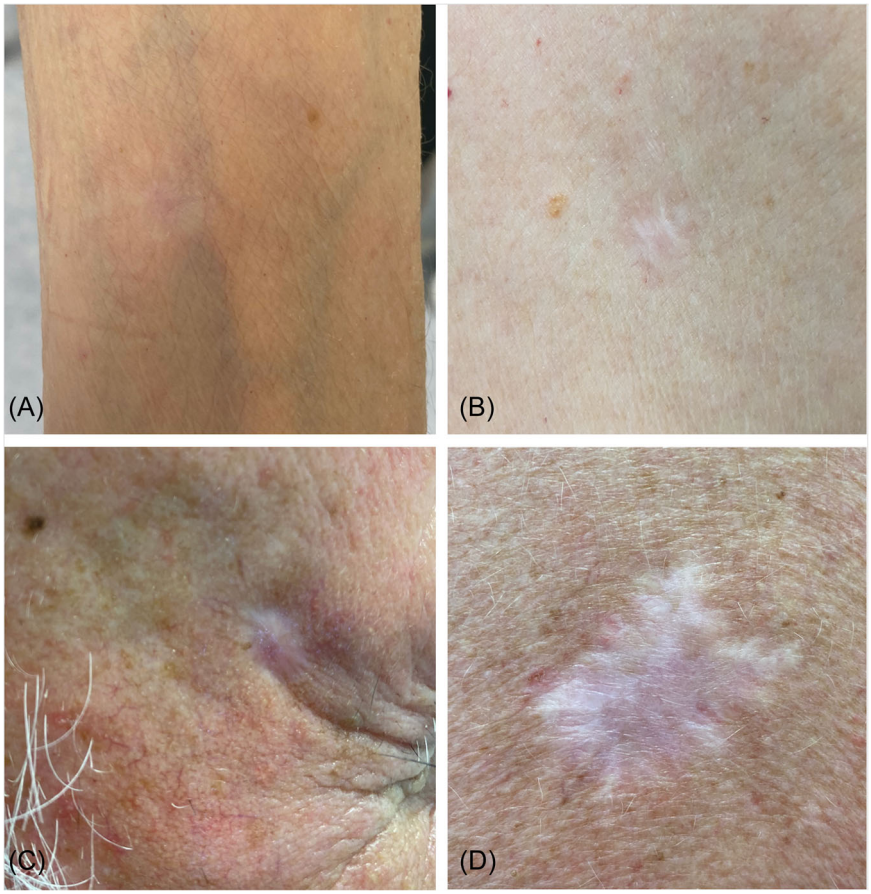


**FIGURE 4** Typical images (taken with an iPhone 12 Pro Camera; [Apple Inc.]) of scarring on the 4-point scale after 12 months (A) 0 = absent; (B) 1 = mild; (C) 2 = moderate; (D) 3 = severe.

mainly occur in the margins of the lesion. Another fact supporting this theory is that in all patients who had a suspected ITC on OCT and who agreed to histological confirmation, the suspected ITC was proven histologically. Unfortunately, not all patients with ITC on OCT agreed to gain histologic backup. Furthermore, the only study reporting a similar ITC rate was also performed using OCT.[12]

Although we expected that the inclusion of patients with anticoagulation, immunosuppression, and any location of BCC would lead to detection of more ITC, in comparison to previously performed studies,[4,5] the multivariate analysis disproved this assumption eventually. Moreover, both characteristics, the BCC subtype and tumor thickness were found to not have a significant impact on the rate of ITC, whereas Markowitz et al.[12] described an association between iBCC and higher ITC rates. However, in our trial, there were only few iBCCs and we only included BCCs with a tumor thickness up to a 1.2 mm. Therefore, a larger cohort with more iBCCs is necessary to identify possible factors which may influence ITC. We think the BCC subtype is of paramount importance as there are often mixed subtypes in one lesion, we classified the BCCs according to the predominantly subtype present. Laser therapy might not be used to treat aggressive subtypes like iBCCs. Identification of the maximum tumor thickness of BCC, which can be treated sufficiently with the Nd:YAG laser might also be a point of interest and a critical topic for subsequent studies.

The ITC rate after 12-month FU was significantly lower compared to 3-month FU suggesting that if ITC is present, it might be detected at an early stage. Reversely, most patients who achieved tumor clearance after 3-month FU, also remained tumor-free in the long term. On the other hand, there are BCCs that do not respond to laser therapy at all—even after multiple treatments. Future studies are of need, to identify possible determining factors for lack of response of laser therapy in some BCC lesions. To reduce ITC rates eventually, OCT-mapping before laser therapy to clearly define the margins may be a useful approach.[26] Another approach to reduce the rate of ITC in the margins, is to plan a bigger overlap of the laser area and the bordering healthy skin in advance.

In our study, the Nd:YAG laser therapy of BCCs is associated with worse cosmetic outcome than in previous studies, even though we used the same laser setting and the same laser device.[12,13,17] It can be speculated that different locations of the investigated BCCs require more refined laser settings. In contrast to other studies[4,5] laser therapy was implemented on any location. Surprisingly, the cosmetic outcome and patient satisfaction did not correlate: This could be due to the age (median 71 years

**TABLE 4** Comparison of patient satisfied and not satisfied with treatment.

| | Yes ($n = 35$) $n$ (%) | No ($n = 10$) $n$ (%) | $p$ Value |
|---|---|---|---|
| Incomplete tumor clearance | | | |
| Incomplete tumor clearance at 3 months | | | 0.467 |
| Yes | 12 (70.6) | 5 (29.4) | |
| No | 23 (82.1) | 5 (17.9) | |
| Patient characteristics | | | |
| Age of patient, median (Q1, Q3) | 75.0 (68.5, 78.0) | 71.0 (63.5, 76.0) | 0.594 |
| Sex of patient | | | 0.476 |
| Male | 20 (83.3) | 4 (16.7) | |
| Female | 15 (71.4) | 6 (28.6) | |
| Immunosuppression | | | 1.000 |
| No | 31 (77.5) | 9 (22.5) | |
| Yes | 4 (80.0) | 1 (20.0) | |
| Anticoagulation | | | 1.000 |
| No | 22 (75.9) | 7 (24.1) | |
| Yes | 13 (81.2) | 3 (18.8) | |
| Side effects | | | |
| Paint during treatment, median (Q1, Q3) | 6.0 (4.0, 7.0) | 7.0 (4.5, 9.8) | 0.144 |
| Treatment outcome | | | |
| Best cosmetic outcome | | | 0.559 |
| Without/mild scarring | 21 (80.8) | 5 (19.2) | |
| Moderate/severe scarring | 7 (100.0) | 0 (0.0) | |
| Worst cosmetic outcome | | | 0.639 |
| Without/mild scarring | 16 (88.9) | 2 (11.1) | |
| Moderate/severe scarring | 12 (80.0) | 3 (20.0) | |

in our study), as well as the fact that the patients were spared surgery or topical treatment for weeks. Furthermore, the patients positively appreciated that the procedure of combining diagnosis and treatment saved a lot of time. This was also observed by Markowitz et al.[17] Patient satisfaction is lowest when the procedure is performed on the lower leg compared to other sites. Interestingly, this result can also be observed in surgery or after trauma.[27]

## CONCLUSION

Our study was able to demonstrate, that Nd:YAG laser treatment for BCC shows significantly higher rates of ITC in an unselected cohort compared to previously conducted studies. The cosmetic outcome after laser treatment may be worse than previously stated. ITC rates were not influenced by histological BCC subtype and/or the OCT-tumor thickness. ITC were found mainly in the marginal area of the lesions. Therefore, further studies are required to identify possible determining factors for ITC in BCC.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

### ORCID

*Pelinsu Yilmaz* http://orcid.org/0000-0002-7113-7560
*Janis Thamm* http://orcid.org/0000-0001-6205-7959
*Stefan Schiele* http://orcid.org/0000-0003-2054-9052
*Julia Welzel* http://orcid.org/0000-0002-6099-7418
*Sandra Schuh* http://orcid.org/0000-0002-1470-7619

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