

## ORIGINAL ARTICLE

# The efficacy and the adverse reactions of laser-assisted tattoo removal – a prospective split study using nanosecond and picosecond lasers

W. Bäumler,  C. Breu, B. Philipp, B. Haslboeck, M. Berneburg, K.T. Weiß

Department of Dermatology, University of Regensburg, Regensburg, Germany

\*Correspondence: W. Bäumler. E-mail: wolfgang.baemler@ukr.de

## Abstract

**Background** Laser pulses with nanosecond duration (NSL) have been the golden standard to destroy the pigment particles in skin. It is still controversially discussed whether picosecond pulses (PSL) are superior for tattoo removal.

**Objectives** To compare the efficacy and the adverse reactions of nanosecond and picosecond laser pulses in a comparative study.

**Methods** The prospective study included 23 subjects with 30 black or coloured tattoos, which were split into two halves treated with either a new PSL (532, 1064 nm) or standard NSL (694 nm). The lasers were applied at regular time intervals of 4 weeks for up to eight treatments. Tattoo clearance (primary endpoint), pain and adverse reactions (secondary endpoints) were appraised by physicians, blinded observers, and by subjects. The extent and duration of adverse reactions were additionally assessed by using a questionnaire and photo-documentation after each treatment session.

**Results** The tattoo clearance appeared to be more effective for PSL compared to NSL but without statistical significance ( $P > 0.05$ ). Pretreated tattoos responded better to laser treatments than previously untreated tattoos. Subjects felt significantly less pain with PSL than with NSL ( $P < 0.001$ ). Transient adverse reactions were statistically less pronounced lasting shorter for PSL as for NSL, especially blistering, pruritus, and burning sensation. Hypopigmentation appeared after NSL treatments only, whereas hyperpigmentation was caused by both lasers. No scarring was detected with either laser.

**Conclusions** Both laser systems enable acceptable clearance of most tattoos in the present study. PSL cause less collateral skin damage as compared to NSL.

Received: 9 June 2021; revised: 10 August 2021; Accepted: 18 August 2021

## Conflict of interest

The authors declare no conflict of interest.

## Funding sources

The picosecond laser device was provided by Alma Laser Ltd. for the length of the study.

## Introduction

Tattooing is an ancient procedure to stain the skin of humans and its history goes back thousands of years.<sup>1</sup> Nowadays, the western world considers tattoos as decorative body art and everybody, usually tattooists in tattoo parlours, perform tattooing. In the past decades, tattooing has become increasingly popular and surveys revealed that in the USA 29% of population has one tattoo at least (2016),<sup>2</sup> in France 17% (2019),<sup>3</sup> Germany 20% (2019),<sup>4</sup> Brazil 22% (2019),<sup>5</sup> and China 12% (2019).<sup>5</sup>

Trial registration DRKS00025487

The trial started in September 2019 and was thus retrospectively registered.

About 5% of tattooed individuals at least desire tattoo removal<sup>6</sup> that requires an effective and safe procedure. Surgical excision may remove a tattoo completely, but it leaves scars, therefore limited to small tattoos.<sup>7</sup> The first laser treatments of tattoos were published by Goldman and co-authors in the Journal of Investigative Dermatology in 1965.<sup>8</sup>

The principle of selective photothermolysis should work for the destruction of tattoo pigment particles in the dermis that leads to fading of a tattoo colour.<sup>9–11</sup> Due to the small size of pigment particles, the principle would require short pulse duration of nanoseconds at least. In addition to short pulse duration, the fragmentation of pigment particles requires a very high laser intensity of laser pulses.

Since the work of Goldman 1965, various clinical studies provided evidence that nanosecond pulses of Q-switched lasers may be effectively and safely applied for tattoo removal but tattoo clearance is frequently incomplete despite a high number of consecutive treatments.<sup>12,13</sup> Therefore, the use of shorter pulse durations in the picosecond range at higher intensities was aimed to overcome such incomplete tattoo clearance.<sup>14</sup> The application of picosecond laser pulses was also mentioned to provide better results not only in black tattoos but also in coloured tattoos.<sup>15–21</sup>

At present, only a few studies exist that compare the nanosecond pulses and picosecond pulses in a prospective clinical study of tattoo removal, unfortunately with some contradictory findings.<sup>20,22,23</sup> One clinical study showed that picosecond pulses are not superior to nanosecond pulses after two consecutive laser treatments.<sup>24</sup> Another study with one to four laser treatments yielded statistically significant superiority of the picosecond lasers compared to the nanosecond laser for tattoo clearance, but not for polychromic tattoos.<sup>20</sup> A study protocol with four consecutive treatments revealed also a superiority of picoseconds as compared to nanoseconds, but now also for polychromic tattoos.<sup>22</sup>

The present clinical study compared a standard nanosecond Q-switched laser (ruby laser), used for tattoo removal for decades, and a picosecond laser (Nd:YAG laser) using a split-tattoo protocol. One half of each tattoo was treated with nanosecond laser, the other half with picosecond laser. This study investigated tattoo clearance for both lasers with up to 8 consecutive sessions, which may represent a typical number in tattoo removal regardless of the laser device used.

The goals of the present study were the comparison of efficacy in removing tattoos for nanosecond and picosecond lasers as well as an in-depth analysis of adverse reactions in the course of the study. The evaluations were based on the study physicians, three blinded observers (dermatologists), and the treated subjects who received a questionnaire after each single treatment session.

## Material and methods

### Study population and baseline characteristics

The study included 23 subjects with overall 30 tattoos consisting of three amateur tattoos and 27 professional tattoos. The majority of subjects were female ( $N = 20$ ) and the mean age of all subjects was of  $33.2 \pm 9.3$  years (range 22–59). The skin type of the subjects was II (32%), III (60%), or IV (8%) according to Fitzpatrick classification.

When the subjects showed up for the first treatment, the age of tattoos ranged from 3 to 39 years with a mean value of  $13.4 \pm 7.1$  years, of which 6 tattoos were pretreated and 24 were not pretreated. The colour of the tattoos was black ( $N = 24$ ) or multi-coloured ( $N = 6$ ) with colours red, green, blue, and pink. The tattoos were located on the arms, legs, head/neck, or trunk

with sizes that ranged from small ( $<25 \text{ cm}^2$ ) to large ( $>100 \text{ cm}^2$ ).

### Laser devices and treatment

A picosecond Nd:YAG laser (PicoClear, Almalaser, Germany) with two wavelengths at 532 or 1064 nm (PSL-532, PSL-1064) delivering pulse durations of 300 or 350 ps, respectively. A nanosecond Ruby laser (Sinon, Almalaser, Germany) with a wavelength of 694 nm and a pulse duration of 20 ns (NSL). Before treating the complete tattooed skin area, a small test treatment was performed to find the appropriate radiant exposure ( $\text{J/cm}^2$ ) by appraising immediate skin reaction (whitening).

### Study design and evaluation

This was a prospective, self-controlled clinical study that compared the efficacy of tattoo removal using two different laser devices. Prior to treatment, each tattoo was randomly split into two equally sized parts, one part was treated with PSL and the other with NSL. On the PSL side of each tattoo, the black part of tattoos was treated with PSL-1064 and any coloured part with PSL-532 only. On the NSL side of each tattoo, this part was treated with NSL regardless of the colour. The primary endpoints of the study were defined as assessment of the clearance of black tattoos with NSL compared to PSL-1064 and the clearance of coloured tattoos with NSL compared to PSL-532.

Secondary endpoints were pain, and the rate and extent of adverse reactions in relation to the respective laser device. The treatments for all subjects were performed at a time interval of 4 weeks. Since the NSL is frequently assumed to require more treatment sessions than for PSL, the tattoo treatments involved up to maximal eight sessions to receive a preferably complete picture of tattoo clearance for both lasers. The treatment was stopped in case no further improvement was observable. The number of treatments was the same for NSL and PSL for each tattoo.

Exclusion criteria were increased sensitivity to light, scars or florid inflammation of the tattooed skin or area immediately surrounding it, pregnant and lactating females. Prior to the first treatment, the patients were given verbal and written information about the course of the study, potential complications and therapeutic alternatives. The trial was conducted in accordance with the Declaration of Helsinki of 1964 after receiving approval from the ethics committee of the University Medical Centre Regensburg, Germany (approval number: 19-1468-101).

Three dermatologists, not involved in laser treatments, acted as independent blinded observers. They compared baseline image (taken prior to treatment) with post-treatment tattoo image (2–3 months after last treatment) grading the clearance of a tattoo in percent using the following scale: 5 = poor clearance ( $<25\%$ ), 4 = fair clearance ( $25\%–49\%$ ), 3 = good clearance ( $50\%–74\%$ ), 2 = excellent clearance ( $75\%–94\%$ ), and 1 = almost complete clearance ( $>94\%$ ). All tattoos were photographed

before and after each treatment session using a digital camera (Canon EOS D80, Tokyo, Japan).

Subjects were asked to assess the pain of each laser treatment using scores of a visual analogue scale (VAS) ranging from 0 to 10 immediately post treatment. All subjects received a questionnaire after each treatment session, in which they were asked to appraise the success of each treatment session in regard to each laser modality. They used grades to value the treatment response of their tattoos at follow-up visits ranging from 1 (excellent), 2 (good), 3 (moderate), 4 (fair), 5 (poor), and 6 (no effect). They also documented the occurrence and duration of adverse reactions with the help of a checklist. Subjects also took photographic images at home to document skin reactions related to laser treatments.

### Skin cooling and anaesthetics

In two consecutive treatments during the study, subjects received two different procedures prior or during laser treatment. First procedure was the application of an anaesthetic cream 60 min prior to laser treatment (EMLA, Aspen Germany GmbH, Munich, Germany). Second procedure was skin cooling using a cold air device during the entire laser treatment (Zimmer Cryo6, Neu-Ulm, Germany). The first full treatment was performed with none of these procedures to enable a comparison of pain perception.

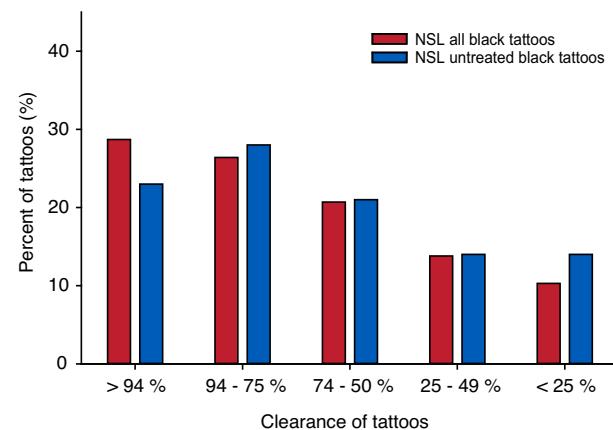
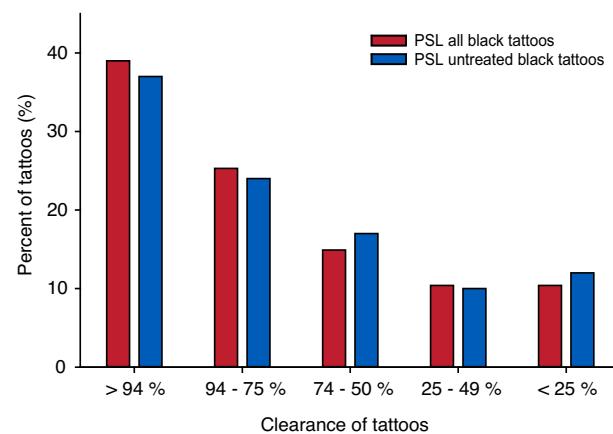
### Statistical analysis

Mean values and standard deviation (SD) were calculated and presented for quantitative characteristics. In particular, the values of tattoo clearance, duration of adverse reactions, and pain scores, presented as mean  $\pm$  SD, were compared for the two laser devices (NSL, PSL) using the non-parametric Mann–Whitney *U*-test or Kruskal–Wallis test. *P*-values were two-sided and considered statistically significant when  $<0.05$ . Assuming a power of 80% and a significance level of 5%, 30 tattoo samples should be sufficient to show a significant difference of tattoo clearance for NSL and PSL. This allows the test of the null hypothesis that PSL is superior to NSL. All analyses were performed using SPSS statistics software version 26.0.0 (IBM SPSS Software, Armonk, NY, USA).

## Results

### Primary endpoint – clearance of tattoos

The mean radiant exposure was  $3.4 \pm 1.3 \text{ J/cm}^2$  (NSL),  $2.1 \pm 0.8 \text{ J/cm}^2$  (PSL-1064), or  $0.8 \pm 0.4 \text{ J/cm}^2$  (PSL-532). The mean number of laser treatments in the study was  $5.5 \pm 1.9$ . In case of blinded observers, the use of PSL-1064 for black tattoos appears to be more effective as compared to NSL (Fig. 1). However, the differences of mean values showed no statistical significance with all *P*-values  $>0.05$  (Table 1) consisting of all groups. Only the direct comparison of tattoos with and without pretreatment yielded a statistically significant difference for each laser ( $P < 0.05$ ). Also, the clearance of coloured tattoos showed no difference for NSL and PSL treatments ( $P > 0.05$ , Table 1).



**Figure 1** Blinded reviewers' assessments are compared for all black tattoos (red bars) and for untreated black tattoos (blue bars) using picosecond pulses (PSL-1064) (top diagram) and nanosecond duration (NSL) (bottom diagram). The differences between all black tattoos and non-pretreated black tattoos are not statistically significant for both lasers ( $P = 0.138$ , PSL) and ( $P = 0.067$ , NSL).

The subjects assessed the clearance of their tattoos rather similar for PSL and NSL and the differences were statistically not significant ( $P > 0.05$ , Table 1). Clearance of some non-pretreated tattoos is exemplarily shown in Fig. 2, for a multi-coloured in Fig. 3, and for a pretreated tattoo in Fig. 4.

### Secondary endpoint – pain assessment

When including all procedures (none, cold air, anaesthetic cream), the NSL treatment revealed a mean pain score of  $5.8 \pm 1.9$  (NSL),  $4.9 \pm 1.7$  (PSL-1064), and  $4.0 \pm 1.8$  (PSL-532). The mean scores of NSL and PSL-1064 were statistically different ( $P < 0.001$ ). The pain scores of no procedure were additionally compared to scores when using cold air or anaesthetic cream (Table 2). The differences were statistically not

**Table 1** Tattoo clearance assessed by blinded observers and patients

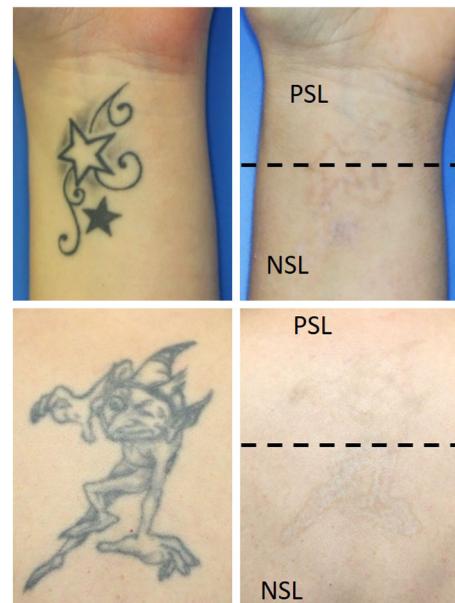
Laser	Blinded observers	Patients' satisfaction
<b>All black tattoos</b>		
NSL	2.5 ± 1.3 <i>P</i> = 0.186	2.9 ± 1.8 <i>P</i> = 0.104
PSL-1064	2.3 ± 1.4	3.1 ± 1.9
<b>Black tattoos non-pretreated</b>		
NSL	2.9 ± 1.3 <i>P</i> = 0.183	3.0 ± 1.0 <i>P</i> = 0.155
PSL-1064	2.6 ± 1.4	3.3 ± 1.1
<b>Black tattoos pretreated</b>		
NSL	1.5 ± 0.5 <i>P</i> = 0.548	2.5 ± 0.8 <i>P</i> = 0.195
PSL-1064	1.4 ± 0.7	2.6 ± 0.4
<b>Coloured tattoos non-pretreated</b>		
NSL	4.1 ± 1.5 <i>P</i> = 0.913	3.2 ± 1.1 <i>P</i> = 0.931
PSL-532	4.0 ± 1.8	4.0 ± 1.6

significant for the use of NSL or PSL-532, with  $P = 0.424$  or  $P = 0.069$ , respectively. In case of NSL-1064, the use of anaesthetic cream significantly reduced the pain when compared to no procedure ( $P = 0.037$ ) and cold air ( $P = 0.032$ ; Table 2).

#### Secondary endpoint – adverse skin reactions

Due to the time span of 4 weeks between two consecutive treatments, the study physicians could document long-lasting adverse reactions only. Mild textural alterations of skin were seen in 4/30 (NSL), 8/30 (PSL-1064), or 2/30 (PSL-532) of tattoos but no scars. Hyperpigmentation showed 2/30 (NSL) or 4/30 (PSL-1064) of tattoos, but none for PSL-532. Hypopigmentation was found for NSL-treated tattoos only (3/30). Examples are shown in Fig. 5, where NSL treatment caused typical hypopigmentation, whereas PSL treatment left hyperpigmentation behind.

Additional information was gained by asking subjects in the follow-up visits and by evaluating all the questionnaires, which were filled by the subjects after every treatment session. The simple evaluation of the frequency of adverse reactions per tattoo revealed that the most common skin reactions after laser treatment of tattoos were erythema and swelling followed by blistering, burning, crusting, bleeding, and pruritus (Fig. 6). Adverse reactions appeared for some tattoos in one treatment session only, for some tattoos more frequently or even in every treatment session. Consequently, a more in-depth evaluation was performed by summing up the frequencies of adverse reactions for all treatment sessions, which involved the treatment of black tattoos using NSL and PSL-1064. The results showed statistically significant differences between NSL and PSL-1064 for blistering ( $P < 0.001$ ) and bleeding ( $P = 0.004$ ), but not for erythema ( $P = 0.880$ ), swelling ( $P = 0.871$ ), pruritus ( $P = 0.499$ ), crusting ( $P = 0.297$ ), and burning ( $P = 0.224$ ). Figures 7 and 8



**Figure 2** Black tattoos (non-pretreated) before (left images) and after five treatment sessions (right images). Nanosecond duration (NSL) below dashed line and picosecond pulses (PSL-1064) above dashed line.

exemplarily show the extent of blistering 2–5 days after a treatment session, which was limited to the NSL-treated skin area.

The mean duration of self-reported adverse reactions such as erythema, swelling, blistering, burning, crusting, and pruritus ranged for both laser devices from about 7 to 15 days (Table 3). The values showed no statistical difference for the laser devices, except for pruritus ( $P = 0.029$ ), which was shorter for PSL-1064 as compared to NSL.

#### Discussion

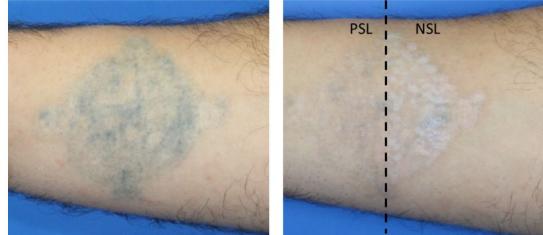
The present study showed that a mean number of about five treatments produced an acceptable clearance of most of the involved tattoos, in particular black tattoos. The laser treatment of black tattoos (non-pretreated and pretreated) showed an excellent clearance (>74%) in 64% (PSL) or 55% (NSL) of tattoos. The PSL-1064 laser seems to be superior to NSL, especially for the group of tattoos with clearance of >94% (Fig. 1). However, the overall differences of the mean results showed no statistical significance when comparing PSL and NSL ( $P > 0.05$ , see Table 1), which refutes the null hypothesis of the primary endpoints. Noteworthy, the light absorption of black pigments varies less than 20% in the spectral range from 400 to 1100 nm, which covers all laser wavelengths used for tattoo removal.<sup>25</sup> Thus, the wavelength of lasers used in the studies for black tattoos should play a minor role if at all. The tattoo clearance after PSL treatments in the present study is comparable to results of other, non-comparative studies using only PSL for tattoo removal.<sup>17,26</sup>



**Figure 3** Multi-coloured tattoo (non-pretreated) before (left) and after five treatment sessions (right). Nanosecond duration (NSL) right to dashed line and picosecond pulses (PSL) left to dashed line. In the PSL area, the black or coloured parts were treated with 1064 or 532 nm, respectively.



**Figure 5** Black tattoo (non-pretreated) before (left) and after five treatment sessions (right). Nanosecond duration (NSL) to the left of dashed line caused hypopigmentation and picosecond pulses (PSL-1064) to the right of dashed line left hyperpigmentation in the treated area.



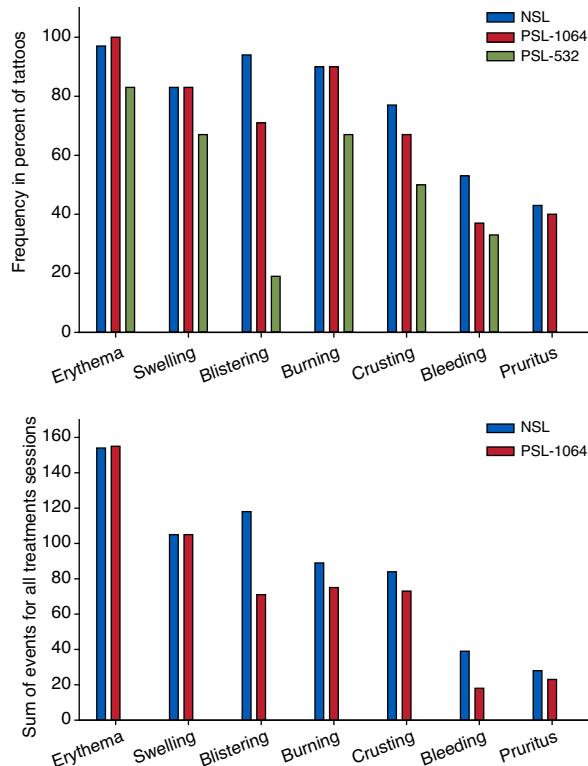
**Figure 4** Black tattoo (pretreated) before (left) and after five treatment sessions (right). Picosecond pulses (PSL-1064) to the left of dashed line caused no persistent adverse reaction. Nanosecond duration (NSL) to the right of dashed line caused typical hypopigmentation.

**Table 2** Pain scores without and with procedures like cold air or anaesthetic cream

Laser	NSL	PSL-1064	PSL-532
Mean values, overall	5.8 ± 1.9	4.9 ± 1.7	4.0 ± 1.8
No procedure	6.0 ± 1.7	5.0 ± 1.6	4.6 ± 1.6
With cold air	5.8 ± 2.0	5.1 ± 1.9	3.9 ± 1.8
With anaesthetic cream	5.4 ± 1.9	4.2 ± 1.8	3.4 ± 1.2

Blinded observers rated the clearance of coloured tattoos as less effective compared to black tattoos, regardless of the respective colour and the laser applied (Table 1). Coloured pigments show various absorption spectra.<sup>27</sup> A few published clinical studies on the clearance of coloured tattoos using different PSL devices exist and the reported results appear somewhat ambiguous.<sup>15,16,22,28</sup> The results of our study match the findings of other comparative studies, which also show comparable clearance of coloured tattoos when treated with PSL or NSL, sometimes with sporadic exceptions for a few colours (Table 4).<sup>20,23</sup>

Pretreated black tattoos responded better to both laser devices with  $P = 0.007$  (NSL) and  $P = 0.025$  (PSL-1064; Table 1) that is



**Figure 6** Adverse reactions were documented in the questionnaire that was filled by the subjects after each treatment session. The results are shown as the frequency of treated tattoos for all lasers (top diagram). The sum over all events during the study is shown for nanosecond duration (NSL) and picosecond pulses (PSL-1064) (bottom diagram).

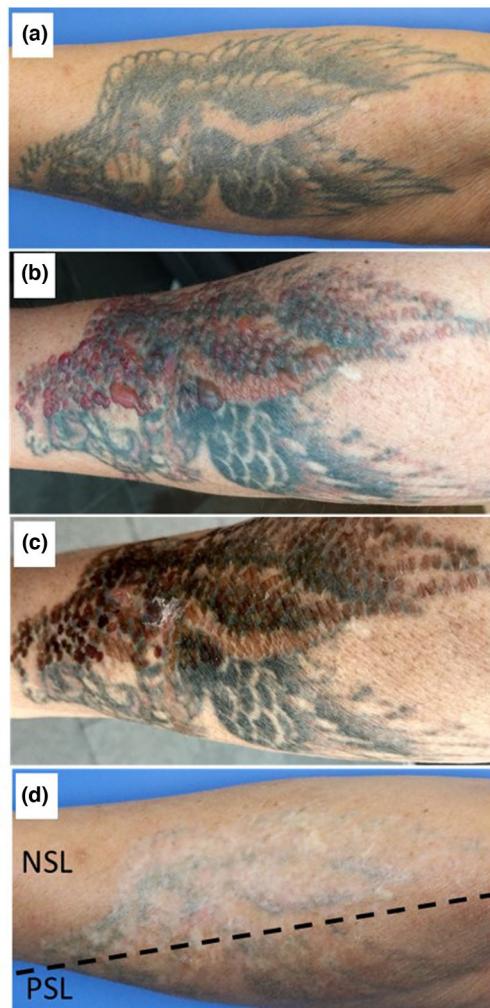


**Figure 7** Black tattoo (non-pretreated) before (left) and after five treatment sessions (right). Nanosecond duration (NSL) below dashed line and picosecond pulses (PSL-1064) above dashed line. An additional photographic image was taken 2 days after second treatment session (middle).

important when comparing the results of the different studies (Table 4). When removing the results of pretreated tattoos from total evaluation (all black tattoos), the percentages of black tattoos with almost complete clearance (>94%) dropped only slightly from 39% to 37% for PSL, but from 29% to 23% for NSL (Fig. 1) indicating an advantage for PSL in treating black tattoos without pretreatment. The percentage of pretreated tattoos in the present study can be considered small (26%) as compared to the other comparative studies with 70%, 71%, or even 100% pretreated tattoos.<sup>20,23,24</sup> One study also observed a different clearance for untreated and pretreated tattoos (Table 4).<sup>20</sup> The percentage of pretreated tattoos is unfortunately missing in another comparative study.<sup>22</sup> In light of the impact of pretreatments on the evaluation of tattoo clearance, pretreatments should be considered an important detail of each study, also when comparing results of different non-comparative clinical studies among each other.<sup>17,26,28,29</sup>

The diverse and sometimes unexpected reactions of tattoo pigments to laser treatments in the different clinical studies remain difficult to explain,<sup>15,18,20,22,23</sup> because tattoo removal with NSL or PSL pulses is based on partially unexplored mechanisms.<sup>10</sup> The use of high intensities of NSL and PSL pulses allows non-linear processes such as two-photon absorption, shock wave generation, and optical breakdown including plasma formation.<sup>10,30,31</sup> All these effects may occur at the same time and their respective extent critically depends on the duration and intensity of laser pulse applied. However, these laser parameters were rather different in clinical studies so far (Table 4).<sup>10</sup> The present study used NSL and PSL devices, whose pulse duration showed a ratio of about 57 to 67. When comparing to the other studies, this value is in the middle of the smallest value of 7 and the highest value of 286 (Table 4). Despite the small number of comparative studies, the available data might indicate that the advantage of PSL over NSL increases with increasing ratio of pulse durations (Table 4). Thus, any superiority of PSL over NSL could be a matter of pulse duration or pulse duration ratio.

In addition, tattoo removal is not only governed by appropriate laser parameters.<sup>10,24,32,33</sup> Fading of tattoo colour requires



**Figure 8** Multi-coloured tattoo (non-pretreated) before (a) and after five treatment sessions (d). Nanosecond duration (NSL) above dashed line and picosecond pulses (PSL) below dashed line. In the area treated with PSL, the black or coloured parts were treated with 1064 or 532 nm, respectively. Additional photographic images were taken 2 days (b) and 5 days (c) after second treatment session.

**Table 3** Duration of adverse reactions (mean days ± standard deviation)

Laser	NSL	PSL-1064	PSL-532	P-value
Erythema	9.7 ± 6.8	9.2 ± 6.7	11.8 ± 6.2	0.229
Swelling	10.4 ± 6.9	10.0 ± 7.0	8.0 ± 3.4	0.648
Blistering	10.0 ± 7.2	11.5 ± 8.0	12.9 ± 6.8	0.232
Burning	9.8 ± 6.5	8.8 ± 7.0	10.9 ± 6.3	0.209
Crusting	11.6 ± 7.6	12.3 ± 7.6	15.1 ± 6.6	0.084
Pruritus	9.9 ± 5.1	7.3 ± 6.6	7.5 ± 0.8	0.029

**Table 4** Overview of parameters and results of comparative studies

Study Year	Pulse duration			Ratio Pulse duration NSL/PSL	Number of treatments	Pretreated tattoos	Results black tattoos	Results coloured tattoos
	NSL	PSL-532	PSL-1064					
present Study	20 ns	300 ps	350 ps	57 67	5.5 ± 1.9 (up to 8)	22%	PSL ≈ NSL	PSL ≈ NSL
Pinto <sup>24</sup> 2017	5 ns	450 ps	450 ps	11	2	70%	PSL ≈ NSL	- <sup>b</sup>
Lorgeou <sup>20</sup> 2018 <sup>a</sup>	5 ns	375 ps 750 ps	450 ps 750 ps	7 – 13	2.0 ± 0.8 (up to 4)	71.4%	PSL > NSL	PSL ≈ NSL <sup>c</sup>
Kono <sup>22</sup> 2020	50 ns	375 ps	450 ps	111 133	4	not specified	PSL > NSL	PSL > NSL <sup>d</sup>
Ross <sup>23</sup> 1998	10 ns	-	35 ps	286	4	100%	PSL > NSL	PSL ≈ NSL

<sup>a</sup>Use of two different PSL. <sup>b</sup>Black tattoos only. <sup>c</sup>Except for blue colours. <sup>d</sup>Statistically not significant for 1064 nm lasers

transportation of fragmented pigment particles away from skin, e.g., via lymphatic system.<sup>10</sup> Pigment capture–release–recapture may ensure macroscopic stability of tattoos and its partial and unpredictable resistance to laser treatments, which might be diverse for tattooed individuals.<sup>34</sup> As for other clinical studies, the laser treatment of tattoos left a number of tattoos behind, whose clearance remains incomplete regardless of the laser type and number of treatments (Figs 2, 3, and 8).

The partially different extent of adverse reactions after treatment with NSL or PSL might be explained when considering studies in ophthalmological microsurgery, which also investigated the use of NSL and PSL devices.<sup>35</sup> The authors found that about 42% (PSL) or 72% (NSL) of laser pulse energy is converted to mechanical energy (shock waves, bubble formation). The authors concluded that the side effects of laser tissue interaction can be considerably reduced by the use of PSL pulses.<sup>36</sup> Histological investigation of tattooed skin samples likewise showed shock waves leaving small vacuoles behind in the dermis, which is clinically perceived as intermediate whitening of the skin.<sup>37</sup>

Firstly, these findings may explain to some extent the smaller pain scores for PSL compared to NSL. It might be assumed that PSL pulses provoke less collateral damage in skin and thereby less pain (Table 2). Secondly, blistering and bleeding should be considered typical signs of laser-induced shock waves in skin, which were significantly less pronounced for PSL ( $P = 0.004$  and  $P < 0.001$ ) as compared to NSL (Fig. 6). The other adverse skin reactions were not significantly different for PSL and NSL, in particular the most frequent reactions erythema and swelling (Table 3).

Treatment of the tattooed skin with either laser has the potential to cause pigmentary alteration because the laser pulses may also interact with the endogenous pigment particles. Surprisingly, none of the tattooed skin showed hypopigmentation after treatment with both PSL wavelengths. Contrary to PSL, NSL treatment caused hypopigmentation after treatment, which is rather common for laser light at 694 nm.<sup>38</sup> However, light absorption of melanin at 532 nm (PSL-532) is higher than for

694 nm (NSL), but the treatment of tattoos with PSL-532 caused also no hypopigmentation. Maybe the low radiant exposure of PSL-532 prevented hypopigmentation but also hyperpigmentation. Other studies report different and inconsistent rates of hypopigmentation for a PSL-532.<sup>15,17,18,20,22</sup>

Contrarily, PSL treatment left a type of darkish hyperpigmentation behind that might be due to excessive melanin and/or ultrafine fragmented black tattoo particles, which are spread in the treated area (Figs 2 and 5). None of the laser treatments in the study entailed scars in the tattooed skin area. After the final treatment, some tattoos showed mild textural alterations. It is often premature to charge the laser treatment with these alterations. The tattooing process itself causes massive skin injuries and the tattoo needles might have caused textural changes, which are hidden by the tattoo colour. Then, the laser treatment removes the colour but simultaneously uncover such textural alterations if caused by the tattooist. The comparison of PSL and NSL regarding the secondary endpoints reveals that the PSL caused less pain and adverse reactions and can be considered smoother and safer for tattoo removal as compared to NSL.

## Conclusions

Picosecond pulses application for tattoo removal should be slightly more effective as compared to NSL application in black tattoos but not in coloured tattoos. When comprising all clinical studies on tattoo removal including the present study, the efficacy for black tattoos and in particular coloured tattoos appears somewhat contradictory that demands further explanation. The PSL is significantly less painful as compared to NSL and the pain scores could be significantly reduced by using an anaesthetic cream. PSL shows a smaller rate of other transient adverse reactions like blistering, bleeding, and pruritus. Due to the individual nature of each tattoo, a split-tattoo study should be mandatory to study the effect of laser parameters like pulse duration on tattoo removal. As all clinical studies show limitations, it would be worthwhile to include a PSL in a comparative

study that provides a pulse duration below 100 picoseconds with a sufficiently high radiant exposure.

## Acknowledgement

The patients in this manuscript have given written informed consent to the publication of their case details. Open access funding enabled and organized by ProjektDEAL.

## References

- 1 Krutak L. The cultural heritage of tattooing: a brief history. In Serup J, Kluger N, Bäumler W, eds. *Tattooed Skin and Health*. Basel, Switzerland: Karger; 2015: 1–5.
- 2 Poll TH. Tattoo Takeover: Three in Ten Americans Have Tattoos, and Most Don't Stop at Just One. The Stagwell Group, 2016. URL <https://theharrispoll.com> (last accessed: 28 September 2021).
- 3 Kluger N, Misery L, Seile S, Taieb C. Tattooing: a national survey in the general population of France. *J Am Acad Dermatol* 2019; **81**: 607–610.
- 4 Borkenhagen A, Mirastschijski U, Petrowski K, Braehler E. Tattoos in Germany: prevalence, demographics, and health orientation. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2019; **62**: 1077–1082.
- 5 Kluger N, Seile S, Taieb C. The prevalence of tattooing and motivations in five major countries over the world. *J Eur Acad Dermatol* 2019; **33**: 484–486.
- 6 Klugl I, Hiller KA, Landthaler M, Baumler W. Incidence of health problems associated with tattooed skin: a nation-wide survey in German-speaking countries. *Dermatology* 2010; **221**: 43–50.
- 7 Wheeland RG, Norwood OT, Roundtree JM. Tattoo removal using serial tangential excision and polyurethane membrane dressing. *J Dermatol Surg Oncol* 1983; **9**: 822–826.
- 8 Goldman L, Wilson RG, Hornby P, Meyer RG. Radiation from a Q-switched ruby laser. Effect of repeated impacts of power output of 10 megawatts on a tattoo of man. *J Investig Dermatol* 1965; **44**: 69–71.
- 9 Gurnani P, Williams N, ALHetheli G et al. Comparing the efficacy and safety of laser treatments in tattoo removal: a systematic review. *J Am Acad Dermatol* 2020.
- 10 Baumler W, Weiss KT. Laser assisted tattoo removal - state of the art and new developments. *Photochem Photobiol Sci* 2019; **18**: 349–358.
- 11 Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983; **220**: 524–527.
- 12 Naga LI, Alster TS. Laser tattoo removal: an update. *Am J Clin Dermatol* 2017; **18**: 59–65.
- 13 Choudhary S, Elsaie ML, Leiva A, Nouri K. Lasers for tattoo removal: a review. *Lasers Med Sci* 2010; **25**: 619–627.
- 14 Izikson L, Farinelli W, Sakamoto F, Tannous Z, Anderson RR. Safety and effectiveness of black tattoo clearance in a pig model after a single treatment with a novel 758 nm 500 picosecond laser: a pilot study. *Laser Surg Med* 2010; **42**: 640–646.
- 15 Alabdulrazzaq H, Brauer JA, Bae YS, Geronemus RG. Clearance of yellow tattoo ink with a novel 532-nm picosecond laser. *Laser Surg Med* 2015; **47**: 285–288.
- 16 Brauer JA, Reddy KK, Anolik R et al. Successful and rapid treatment of blue and green tattoo pigment with a novel picosecond laser. *Arch Dermatol* 2012; **148**: 820–823.
- 17 Kauvar ANB, Keane TC, Alster T. Laser treatment of professional tattoos with a 1064/532-nm dual-wavelength picosecond laser. *Dermatol Surg* 2017; **43**: 1434–1440.
- 18 Bernstein EF, Schomacker KT, Basilavecchio LD, Plugis JM, Bhawalkar JD. A novel dual-wavelength, Nd:YAG, picosecond-domain laser safely and effectively removes multicolor tattoos. *Laser Surg Med* 2015; **47**: 542–548.
- 19 Choi MS, Seo HS, Kim JG et al. Effects of picosecond laser on the multi-colored tattoo removal using Hartley guinea pig: a preliminary study. *PLoS One* 2018; **13**: e0203370.
- 20 Lorgeou A, Perrillat Y, Gral N, Lagrange S, Lacour JP, Passeron T. Comparison of two picosecond lasers to a nanosecond laser for treating tattoos: a prospective randomized study on 49 patients. *J Eur Acad Dermatol Venereol* 2018; **32**: 265–270.
- 21 Saedi N, Metelitsa A, Petrell K, Arndt KA, Dover JS. Treatment of tattoos with a picosecond alexandrite laser: a prospective trial. *Arch Dermatol* 2012; **148**: 1360–1363.
- 22 Kono T, Chan HHL, Groff WF, Imagawa K, Hanai U, Akamatsu T. Prospective comparison study of 532/1064 nm picosecond laser vs 532/1064 nm nanosecond laser in the treatment of professional tattoos in Asians. *Laser Ther* 2020; **29**: 47–52.
- 23 Ross V, Naseef G, Lin G et al. Comparison of responses of tattoos to picosecond and nanosecond Q-switched neodymium: YAG lasers. *Arch Dermatol* 1998; **134**: 167–171.
- 24 Pinto F, Grosse-Bunten S, Karsai S et al. Neodymium-doped yttrium aluminum garnet (Nd:YAG) 1064-nm picosecond laser vs. Nd:YAG 1064-nm nanosecond laser in tattoo removal: a randomized controlled single-blind clinical trial. *Brit. J Dermatol* 2017; **176**: 457–464.
- 25 Han DX, Meng ZG, Wu DX, Zhang CY, Zhu HT. Thermal properties of carbon black aqueous nanofluids for solar absorption. *Nanoscale Res Lett* 2011; **6**: 2–7.
- 26 Nguyen HT, Doan EVL, Tran TNA, Vu TTP, Phan HN, Sobanko JF. Safety and efficacy of tattoo removal using a dual-wavelength 1064/532-nm picosecond laser in patients with Fitzpatrick skin type III and IV. *Laser Surg Med* 2021; **53**: 939–945.
- 27 Baumler W, Eibler ET, Hohenleutner U, Sens B, Sauer J, Landthaler M. Q-switch laser and tattoo pigments: first results of the chemical and photophysical analysis of 41 compounds. *Laser Surg Med* 2000; **26**: 13–21.
- 28 Bernstein EF, Bhawalkar J, Schomacker KT. A novel titanium sapphire picosecond-domain laser safely and effectively removes purple, blue, and green tattoo inks. *Laser Surg Med* 2018; **50**: 704–710.
- 29 Bernstein EF, Schomacker KT, Shang XM, Alessa D, Algizlan H, Paranjape A. The first commercial 730 nm picosecond-domain laser is safe and effective for treating multicolor tattoos. *Laser Surg Med* 2021; **53**: 89–94.
- 30 De Boni L, Misoguti L, Zilio SC, Mendonca CR. Degenerate two-photon absorption spectra in azoaromatic compounds. *ChemPhysChem* 2005; **6**: 1121–1125.
- 31 Karpicz R, Gulbinas V, Stanishauskaite A, Undzenas A. Characterization of bisazo compounds employing ultrafast spectroscopy. *Chem Phys* 2001; **269**: 357–366.
- 32 Humphries A, Lister TS, Wright PA, Hughes MP. Finite element analysis of thermal and acoustic processes during laser tattoo removal. *Laser Surg Med* 2013; **45**: 108–115.
- 33 Ho DD, London R, Zimmerman GB, Young DA. Laser-tattoo removal—a study of the mechanism and the optimal treatment strategy via computer simulations. *Laser Surg Med* 2002; **30**: 389–397.
- 34 Baranska A, Shawket A, Jouve M et al. Unveiling skin macrophage dynamics explains both tattoo persistence and strenuous removal. *J Exp Med* 2018; **215**: 1115–1133.
- 35 Vogel A, Busch S, Parlitz U. Shock wave emission and cavitation bubble generation by picosecond and nanosecond optical breakdown in water. *J Acoust Soc Am* 1996; **100**: 148–165.
- 36 Vogel A, Busch S, Jungnickel K, Birngruber R. Mechanisms of intraocular photodisruption with picosecond and nanosecond laser pulses. *Laser Surg Med* 1994; **15**: 32–43.
- 37 Ferguson JE, Andrew SM, Jones CJ, August PJ. The Q-switched neodymium:YAG laser and tattoos: a microscopic analysis of laser-tattoo interactions. *Br J Dermatol* 1997; **137**: 405–410.
- 38 Piazza H, Meffert H, Uebelhack R. Spectral remittance and transmittance of visible and infrared-A radiation in human skin: Comparison between *in vivo* measurements and model calculations. *Photochem Photobiol* 2017; **93**: 1449–1461.