

# Rapid, High-Fluence Multi-Pass Q-Switched Laser Treatment of Tattoos With a Transparent Perfluorodecalin-Infused Patch: A Pilot Study

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**Background and Objectives:** Perfluorodecalin (PFD) has previously been shown to rapidly dissipate the opaque, white micro-bubble layer formed after exposure of tattoos to Q-switched lasers [1]. The current pilot study was conducted to qualitatively determine if the use of a transparent PFD-infused silicone patch would result in more rapid clearance of tattoos than conventional through-air techniques.

**Materials and Methods:** Black or dark blue tattoos were divided into two halves in a single-site IRB-approved study with 17 subjects with Fitzpatrick skin types I–III. One half of each tattoo served as its own control and was treated with one pass of a standard Q-switched Alexandrite laser (755 nm). The other half of the tattoo was treated directly through a transparent perfluorodecalin (PFD) infused patch (ON Light Sciences, Dublin, CA). The rapid whitening reduction effect of the Patch routinely allowed three to four laser passes in a total of approximately 5 minutes. Both sides were treated at highest tolerated fluence, but the optical clearing, index-matching, and epidermal protection properties of the PFD Patch allowed significantly higher fluence compared to the control side. Standard photographs were taken at baseline, immediately prior to treatment with the PFD Patch in place, and finally before and after each treatment session. Treatments were administered at 4- to 6-week intervals.

**Results:** In a majority of subjects (11 of 17), tattoos treated through a transparent PFD-infused patch showed more rapid tattoo clearance with higher patient and clinician satisfaction than conventional treatment. In no case did the control side fade faster than the PFD Patch side. No unanticipated adverse events were observed.

**Conclusions:** Rapid multi-pass treatment of tattoos with highest tolerated fluence facilitated by a transparent PFD-infused patch clears tattoos more rapidly than conventional methods. *Lasers Surg. Med.* 47:613–618, 2015. © 2015 The Authors. *Lasers in Surgery and Medicine* published by Wiley Periodicals, Inc.

**Key words:** laser tattoo removal; perfluorodecalin; PFD patch; optical clearing; epidermal protection; skin

## INTRODUCTION

Laser-assisted tattoo removal has well-known limitations. Often a lengthy regimen of many treatment sessions

is required. Although a scale has been described that estimates the number of required sessions [2], it is often difficult for the clinician to predict the number of treatment sessions required for satisfactory tattoo fading or clearance [3]. It is not uncommon that 10 or more sessions at 4- to 6-week intervals are required for a proper aesthetic result. This poses significant challenges for subjects and clinicians alike, and is often an inhibiting factor for subjects desiring tattoo removal from actually obtaining it. The R-20 multi-pass technique initially showed promise by allowing several laser passes in a single session by permitting the laser-induced opaque whitening caused by the generation of micro-cavitation bubbles to naturally subside in approximately 20 minutes [4]. This technique has not been widely adopted largely due to workflow limitations; one patient could require an 80-minute treatment session which is impractical in a busy clinical setting. Recently, it was demonstrated that perfluorodecalin (PFD) could rapidly dissipate the opaque, white micro-bubble layer formed after exposure of tattoos to Q-switched lasers, allowing clinically efficient multi-pass treatment [1]. To this end, the present qualitative pilot study was undertaken to determine if rapid multiple laser passes at highest tolerated fluence enabled by a transparent PFD-infused silicone patch might have a similar beneficial effect for laser tattoo removal.

## The Perfluorodecalin Patch

Perfluorodecalin is a stable, metabolically inert fluorocarbon liquid that has excellent optical transparency from the

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UV to the far-IR [5]. It has the unusual properties of simultaneously being both lipophobic and hydrophobic, yet it is freely flowing with an extremely low surface energy that allows it to rapidly wick into porous materials. Its intraocular use assists in the repair of detached retinas. It enhances cosmetic preparations as a skin conditioner and hair detangler, but its high cost has limited more general use.

A well-known property of PFD and similar perfluorocarbons is their ability to dissolve gasses [6]. PFD can absorb half its liquid volume of gaseous oxygen as well as other gases such as nitrogen and steam. This led to its use in first-generation artificial blood substitutes as well as ongoing work in liquid ventilation and related medical applications [6,7]. Since the partial pressure of gas in laser-induced micro-cavitation bubbles is well above the partial pressure of atmospherically equilibrated PFD, the diffusion of gas from micro-bubbles into liquid PFD requires no special handling or degassing requirements.

Although it is a heavy molecule with approximately twice the density of water, PFD readily evaporates when exposed to room air, an effect exacerbated by warm skin. Covering it with a transparent impermeable membrane greatly reduces evaporation. There are also optical index-matching benefits to both the PFD and to the silicone material described below. The Patch has the added benefit of eliminating fumes and back-splatter.

### **Silicone Material, Micro-Perforations, and Gas Absorption**

PFD is insoluble in virtually all liquids, gels, waxes, and polymers. A solution to this problem was simply to perforate medical-grade silicone gel with a multiplicity of fine holes, and allowing the PFD to mechanically reside in them. PFD rapidly wicks into the perforations, and then readily wicks back out onto the surface of the skin.

### **Index Matching, Optical Clearing, and Fluence**

The index of refraction of human epidermal tissue was measured by Ding et al. to vary from 1.44 at 600 nm to 1.42 at 1064 nm [8]. The indices of refraction of perfluorodecalin and the transparent silicone material are 1.31 and 1.40, respectively. This provides good optical index matching that allows efficient coupling of laser light into the skin despite the presence of the liquid PFD and the silicone Patch itself. A more significant effect appears to be optical clearing induced by the PFD. Littlejohn et al. have recently exploited this effect in a striking series of confocal microscopy studies of plant leaves [9]. When an opaque plant leaf is briefly immersed in PFD, it becomes sufficiently transparent to read text through it. Water and other common solvents do not produce this effect.

The optical clearing effect of the PFD Patch may have significance in laser tattoo removal for several reasons. The reduction in optical scattering allows more photons to penetrate into the skin to interact with deeply residing ink particles, and reduces the local fluence near the skin surface compared to more highly scattering conventional treatment. This effect would also reduce potentially

damaging epidermal thermal effects by reducing heat generated superficially by the laser, as well as thermally coupling heat that is generated into the bulk material of the silicone.

## **MATERIALS AND METHODS**

### **Choice of Laser**

A conventional nanosecond pulse duration Q-switched Alexandrite 755-nm laser (Candela Alex TriVantage, Wayland, MA) was selected for use in this study. While several laser wavelengths may be used to treat black and dark blue ink, 755 nm is well recognized as being clinically effective in achieving clearance of such tattoos [3,10]. The selection of wavelength chosen for this particular study design was based simply on general availability and well-established clinical efficacy. The PFD Patch was designed to have no clinical effect on wavelength or spot size selection; its optical clearing effect was however clinically observed to allow substantially higher maximum tolerated fluence. This was based on standard clinical signs and symptoms, as described below.

### **Subject Selection**

This was an Allendale IRB-approved, single-site, split-side, prospective pilot study to evaluate the efficacy and safety of a transparent PFD patch as an accessory to laser tattoo removal for accelerated clearing of blue or black tattoos. Twenty adult subjects, Fitzpatrick skin types I–III, were enrolled in the study, with 15 remaining (two subjects had two tattoos) for five or more treatment sessions at approximately 4-week intervals. Inclusion criteria included subjects 18 years of age with previously untreated tattoos less than 100 cm<sup>2</sup> in size consisting of dark blue or black ink, Fitzpatrick Skin Type I–III, no tan in the treatment area and no contraindications for participation in a clinical trial or treatment with a Q-switched laser. Subjects with a history of oral gold therapy, hypertrophic or keloidal scarring, use of oral retinoids within the previous 12 months, or who were pregnant, or breastfeeding were excluded.

### **Treatment Protocol**

Informed consent was obtained as per standard protocol. Characteristics including age, gender, Fitzpatrick skin type, tattoo site, and color(s) present in the tattoo were documented during the enrollment session. One half of the tattoo was randomly assigned laser treatment using the PFD Patch; the other half received conventional laser treatment through air without the Patch and served as the control.

Lidocaine HCl 1% with or without epinephrine 1:100,000 was injected at the treatment site on all subjects throughout the study. PFD was applied to the skin and the Patch was applied approximately 5 minutes prior to laser treatment. No PFD or occlusive dressings were used on the Control half. Subjects and staff used appropriate laser-safe eyewear and all laser-safe precautions were taken. Standard unpolarized flash photographs were taken for all subjects

at each visit before treatment, showing Patch placement, and immediately post-treatment.

The PFD Patch side received rapid multiple laser passes as clinically indicated, typically 3 or 4, with an average of 3.6. The Control half received a single laser pass due to the immediate development of persistently opaque epidermal whitening following exposure to laser energy rendering additional treatments impossible. Both sides of the tattoo were treated at the maximum-tolerated fluence as determined by epidermal whitening without frank, clinically apparent blister formation. Treatment through the patch allowed higher treatment fluence in all subjects relative to control. The Patch was lifted between passes and additional PFD was reapplied with a foam-tipped swab (MG Chemicals, Burlington, Canada) to replenish any liquid that may have been absorbed into the skin. In cases where some epidermal whitening developed despite treatment through the patch, with reapplication of liquid PFD this whitening typically resolved rapidly. The Patch was repositioned immediately after reapplication of liquid PFD to minimize evaporation and additional laser treatment was administered without further delay.

Upon completion of each treatment, subjects were given complete wound care instructions including clinic contact information. Aquaphor<sup>®</sup> (Beiersdorf, Wilton, CT) was applied, and Tegaderm<sup>™</sup> frame-style film dressings were applied over the treated area (3M, St. Paul, MN). The presence of side effects and adverse events was assessed and recorded for both Patch and Control sites immediately after treatment and at each visit.

Repeat treatments were performed at 4- to 6-week intervals until the tattoo was either fully resolved on the Patch side or until no further clinical benefit was deemed likely. At that time, subjects continued to receive laser treatments to the Control side until the tattoo reached the maximal perceived clinical benefit. It is worth noting that although subjects were given the choice of continuing treatment with or without the Patch on the Control side after the Patch side had cleared, all chose to continue with the Patch.

## RESULTS

In 11 out of 17 tattoos, those treated through the PFD Patch showed more rapid clearance with higher subject satisfaction than standard through-air treatment (Table 1). The Patch allowed three or four rapid multiple passes in all subjects as opposed to only a single pass on the Control side. The Patch also allowed an increased fluence to be delivered relative to Control by a factor of 1.5× to 1.8×, despite multiple laser passes, without an increase in adverse events. These anticipated adverse events were mild to moderate in severity and included erythema, edema, pain, and crusting. The incidence of anticipated adverse events was the same for both the Patch and Control sides of the tattoos. Blister formation was reported by 2 of the subjects, and transient hypopigmentation by 3 of the subjects, all of which resolved completely and without sequelae. No scarring, textural changes, or unanticipated

adverse events were observed. As one example, Figure 1 shows subject 15 at: baseline, immediately after treatment 1, and 4 weeks after treatment 5. Whitening was significantly reduced with the Patch and accelerated clearing is evident.

There was a wide array of responses ranging from dramatic superiority after only two treatment sessions with over 90% clearance on the Patch side compared to less than 20% on the Control side, to marked superiority which became apparent after a few treatments, to cases in which superiority of the Patch was not demonstrated. Typical positive results are shown in Figure 2. Even in cases where superiority of clearance relative to Control was not demonstrated, the Control side never achieved better clearance than the Patch side.

## DISCUSSION

This proof-of-concept pilot study was designed to qualitatively compare the effect of rapid, multiple Q-switched laser passes performed at highest tolerated fluence in conjunction with an optical clearing and index matching PFD Patch relative to standard Q-Switched laser treatment on the clearing of tattoos. Quantifying the improvement in rate of clearance, and partitioning the benefit of multiple passes and/or higher fluence on outcomes were beyond the scope of the study design. However, this study demonstrated that the PFD Patch, when used in conjunction with a Q-switched laser, produces a beneficial effect with respect to clearance of blue and black tattoo ink relative to standard treatment protocols.

Variability of tattoo response to Q-switched laser treatment has long been recognized. Some of the factors implicated in this phenomenon include the age of the tattoo, the composition and depth of the ink, location on the body, smoking status, and professional versus amateur application. Future studies that explore these parameters as they relate to PFD Patch efficacy are clearly warranted, as are studies that evaluate the PFD Patch in conjunction with Q-switched lasers of other wavelengths and pulse durations in both the nanosecond and picosecond range.

Just as there are many factors affecting the speed and efficacy of laser tattoo removal in general, there appear to be several mechanisms at play with the use of the PFD Patch. The first involves the unusual ability of PFD itself to absorb gas [6,7]. When a tattoo is exposed to the high optical energy of a laser pulse, stress waves, and cavitation bubbles are formed [11]. This effect is observed clinically as whitening or frosting over the tattoo. The apparent white layer is composed of microscopic bubbles formed nearly instantaneously as energy absorbed by the ink particles is transferred to surrounding tissue. The white layer is highly optically scattering and thus effectively opaque. Further laser passes are ineffective because light can no longer penetrate sufficiently to interact with the pigment. The first mechanism that the PFD Patch facilitates is the direct absorption of the gas within the bubbles. Gas preferentially diffuses and absorbs into PFD. Also, PFD contained in the most distal

**TABLE 1. Summary of Subject Demographics and Observations**

Sub #	Tattoo location	Fitzpatrick skin type	Sex	Age	Spot size patch/control (mm)	Max fluence patch/control (J/cm <sup>2</sup> )	#Passes (patch/control)	Improved clearing?
01	Wrist	II	F	32	4/3	9.5/5.5	3	Y
02	Chest	III	M	42	4/3	9.5/5.5	4	Y
04	Shoulder	III	M	34	4/3	9.5/5.0	3	Y
05	Wrist	III	F	34	4/3	9.5/5.5	4	Y
06a	Wrist	II	F	36	4/3	9.5/5.5	4	Y
06b	Forearm	II	F	36	4/3	9.5/5.5	3	Y
07	Lower back	I	F	40	4/3	9/5.5	3	Y
08	Lower back	III	F	32	4/3	9.0/5.5	4	N
09	Neck	I	F	34	4/3	9.0/5.5	4	Y
10	Forearm	III	M	38	4/3	9.0/5.0	3	N
11	Abdomen	I	F	33	4/3	9.0/5.0	3	Y
12a	Shoulder	II	F	36	4/3	9.0/5.0	3	N
12b	Abdomen	II	F	36	4/3	8.0/5.0	4	N
14	Foot	III	F	42	4/3	8.0/5.0	3	N
15	Neck	II	F	28	4/3	9.0/5.5	4	Y
18	Hip	II	F	26	4/3	8.0/5.5	3	N
19	Forearm	II	F	25	4/3	9.0/5.5	3	Y
Total subjects						N = 17		
Total tattoos treated						N = 19		
Fitzpatrick skin types						I – 4		
						II – 6		
						III – 7		
Age range						25–42		
Sex						M – 3		
						F – 14		

part of the perforations is at a lower partial pressure than that at the surface in direct contact with the cavitation bubbles, which drives the dissolution of gasses into the PFD.

A second mechanism is optical clearing [12]. PFD is a very mobile fluid that readily fills voids and wicks into porous materials [9,13]. As the opaque bubble layer dissipates, optical clearing may become the dominant mechanism allowing photons to penetrate more deeply into the tissue [14]. The laser may have improved efficacy if its light reaches deep ink particles due to a reduction in optical scattering; this may lead to better treatment of recalcitrant

tattoos. But optical clearing also has a counterintuitive effect; it reduces the local fluence in the upper layers of the skin precisely because it reduces scattering. This allows more photons to penetrate more deeply where recalcitrant ink tends to reside, but also appears to require a higher incident fluence to compensate for the reduction in local fluence in the uppermost layers of the skin. This is consistent with our clinical observation that the Patch allows higher tolerated fluence when compared to through-air treatment of the same tattoo. We note that even as the Patch significantly increases the maximum tolerated fluence, this increase did not result in increased side effects.



**Fig. 1.** (A) Tattoo from subject 15 at baseline. (B) The PFD Patch on the left side of the tattoo reduces whitening allowing four laser passes in a few minutes. (C) 4 weeks after the 5th treatment session.



Fig. 2. (A) Subject 6A at baseline, and after nine treatments. (B) Subject 6B at baseline, and after eight treatments. (C) Subject 7 at baseline, and after eight treatments. (D) Subject 11 at baseline, and after seven treatments. (E) Subject 1 at baseline, and after seven treatments. (F) Subject 2 at baseline, and after eight treatments. (G) Subject 9 at baseline, and after two treatments.

A third mechanism is index matching. The index of refraction of human epidermal tissue was measured by Ding et al. to vary from 1.44 at 600 nm to 1.42 at 1064 nm [8]. The index of refraction of perfluorodecalin and the transparent silicone material are 1.31 and 1.40, respectively. This provides optical index matching that allows efficient optical coupling of laser light into the skin despite the presence of the Patch.

A fourth mechanism is thermal protection of the epidermis by the bulk transparent silicone material of the PFD Patch itself as well as the high heat capacity of

PFD relative to air. As the Patch is placed on the skin, air is excluded from the Patch-skin interface providing good thermal coupling from the epidermis through the PFD into the silicone. Clinically, we also note that fumes and debris are eliminated. This is extremely important from a perspective of both patients and staff as laser-plume has been well documented to contain noxious materials [15,16]. It is also important to note that, despite greater total energy application on the PFD-treated side on account of both multiple passes and increased fluence, there were no increases in adverse

events or delay in recovery time associated with use of the PFD patch.

## CONCLUSIONS

Rapid multi-pass treatment of tattoos with highest tolerated fluence facilitated by a transparent PFD-infused patch clears tattoos more rapidly than conventional methods. We observed that even with multiple laser passes, the highest tolerated fluence could be safely increased by a typical factor of  $1.5\times$  to as high as  $1.8\times$  with the PFD Patch as compared to conventional treatment through an air-skin interface on the Control side of the same tattoo using a 755-nm Q-switched alexandrite laser. The incidence of anticipated adverse events was no different between treatment and control. No unanticipated adverse events were observed. Although this study was limited by its modest sample size and by the use of only one laser wavelength and pulse duration, the potential benefit of the PFD Patch with other wavelengths and pulse durations (including picosecond lasers) warrants further investigation.

## AUTHOR CONTRIBUTIONS

Dr. Biesman and Ms. Costner had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design were done by Dr. Biesman. Acquisition of data was performed by Dr. Biesman and Ms. Costner. Drafting of the manuscript was done by Dr. Biesman and Dr. O'Neil. Critical revision of the manuscript for important intellectual content was performed by Dr. Biesman, Dr. O'Neil. Study supervision was done by Dr. Biesman.

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