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# Selective removal of stratum corneum by microdermabrasion to increase skin permeability

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ABSTRACT

This study sought to determine if microdermabrasion can selectively remove stratum corneum to increase skin permeability. Although, microdermabrasion has been used for cosmetic treatment of skin for decades, no study has assessed the detailed effects of microdermabrasion conditions on the degree of skin tissue removal. Therefore, we histologically characterized the skin of rhesus macaques and human volunteers after microdermabrasion at different conditions. Using mobile tip microdermabrasion, an increase in the number of treatment passes led to greater tissue removal ranging from minimal effects to extensive damage to deeper layers of the skin. Of note, these data showed for the first time that at moderate microdermabrasion conditions selective yet full-thickness removal of stratum corneum could be achieved with little damage to deeper skin tissues. In the stationary mode of microdermabrasion, selective stratum corneum removal was not observed, but micro-blisters could be seen. Similar tissue removal trends were observed in human volunteers. As proof of concept for drug delivery applications, a model fluorescent drug (fluorescein) was delivered through microdermabraded skin and antibodies were generated against vaccinia virus after its topical application in monkeys. In conclusion, microdermabrasion can selectively remove full-thickness stratum corneum with little damage to deeper tissues and thereby increase skin permeability.


## 1. Introduction

Microdermabrasion is an FDA approved process first introduced in 1985 and is a popular method used to treat scars, acne and other cosmetic-dermatologic conditions (Spencer, 2005). Recently there has been interest in using microdermabrasion to enable transdermal drug delivery. It is known that skin's top-most layer, the stratum corneum is the main transport barrier to delivery of drugs and vaccines across the skin and that removal of stratum corneum dramatically increases skin permeability (Prausnitz and Langer, 2008). Accordingly, to enable transdermal drug delivery various approaches have been investigated for the selective removal of stratum corneum to increase drug transport without damaging living cells of the viable epidermis layer just beneath the stratum corneum or causing widespread damage that is difficult for the skin to repair rapidly. While tape stripping has been employed to remove stratum corneum in many laboratory studies (Godefroy et al., 2005; Guy and Hadgraft, 2002), thermal ablation and mechanical abrasion have been emphasized for transdermal drug delivery with clinical potential. Thermal ablation of the stratum corneum has been carried out using lasers (Fang et al., 2004a), radiofrequency energy (Sintov et al., 2003) and direct application of heat (Bramson et al., 2003; Arora et al., 2008) while mechanical abrasion of the stratum corneum has been carried out using abrasive-pads (Glenn et al., 2007), blunt-tipped microneedles (Mikszta et al., 2002) and microdermabrasion (Fujimoto et al., 2005; Lee et al., 2006).

Mechanistically, microdermabrasion involves impingement of sharp microparticles on the skin surface, which are then removed under vacuum into a waste container along with the abraded skin tissue. Using microdermabrasion, various researchers have shown increased permeability of freshly excised animal skin to very low molecular weight compounds (<300 Da) recording a 10–20-fold

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flux enhancement of estradiol (Fujimoto et al., 2005), vitamin C (Lee et al., 2003), and 5-aminolaevulinic acid (Fang et al., 2004a). In contrast to microdermabrasion, which uses vacuum to produce flow of microparticles, a related approach called microscission uses a positive pressure to accelerate and impinge microparticles on the skin. Using this approach, lidocaine delivery and blood glucose measurement were demonstrated in human volunteers (Herndon et al., 2004).

Although various studies have shown that microdermabrasion enhances transdermal flux, a significant challenge in the development of microdermabrasion for clinical applications is the limited understanding of the effects of microdermabrasion on skin. Of note, while the different studies have demonstrated flux enhancement, they have not demonstrated full-thickness removal of the stratum corneum layer, which is critical for reproducible and controlled transdermal delivery of large molecular weight compounds and vaccines. Furthermore, a mechanistic understanding is lacking even for cosmetic applications of microdermabrasion for which the device is already approved by the FDA. This is largely because the microdermabrasion device was originally classified as a class-I device, which according to the FDA is a device that presents minimal potential for harm to the user and general controls are sufficient to ensure safety. Consequently the microdermabrasion device never underwent phase-III clinical trials or the associated detailed characterization (Spencer, 2005).

For transdermal drug delivery applications it is important to understand the effects of microdermabrasion on the skin layers such that the full-thickness of stratum corneum can be removed in a controlled fashion with minimum collateral damage to the underlying viable cells of the epidermis. Therefore, in this study we carried out detailed histological examination of the skin after performing microdermabrasion in vivo on the skin of rhesus macaques and human volunteers. Multiple skin biopsies were obtained from the microdermabraded sites and histologically analyzed to assess the effects of microdermabrasion on the different skin layers.

## 2. Materials and methods

### 2.1. Microdermabrasion apparatus

Microdermabrasion was performed using an FDA-approved device (MegaPeel® Gold Series, DermaMed International, Lenni, PA, USA) with disposable microdermabrasion tips having a skin-contacting hole with a 7 mm inner diameter (Fig. 1a). The size and morphology of the aluminum oxide particles (DermaMed International) used for microdermabrasion were determined through scanning electron microscopy (LEO-1530, LEO electron microscopy, Cambridge, England). The particles were found to have highly irregular shapes with sharp edges (Fig. 1b). The largest dimension of the majority of the particles was between 100 and 300 μm, although a small amount of particulate debris (about 1 μm) was also found.

To facilitate microdermabrasion of the same skin area during repeated passes, rectangular polyethylene medical foam tape (TM9716, MACtac, Stow, OH, USA) stencils (55 mm × 30 mm) with rectangular slits (40 mm × 10 mm) were attached to the skin of rhesus macaques and human volunteers. The slits were precisely cut using a computer-controlled $CO_2$ laser (LS500XL. New Hermes, Duluth, GA, USA). For the mobile tip mode, the tips were moved manually back and forth within the slit of the stencil. The slit width of 10 mm closely accommodated the outer diameter of the microdermabrasion tip and thereby facilitated repeated motion over the same path on the skin. For the stationary tip mode, the microdermabrasion tip was placed directly on the skin surface without the use of a stencil.

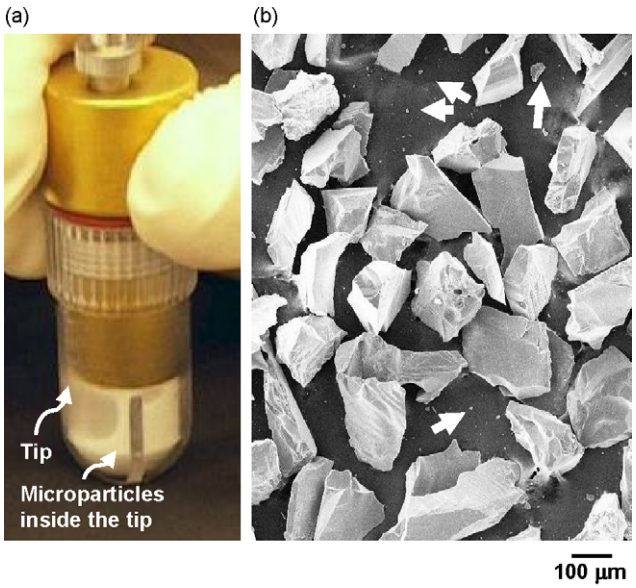


**Fig. 1.** Microdermabrasion tip and particles. A microdermabrasion tip with aluminum oxide microparticles flowing inside the tip (a). Scanning electron microscopy image of aluminum oxide microparticles with a small population of very small particles (pointed to by arrows) (b).

### 2.2. In vivo rhesus macaque microdermabrasion

Microdermabrasion was performed on the backs of rhesus macaque monkeys (Yerkes National Primate Research Center, Emory University, Atlanta, GA) after trimming the hair and cleaning the skin with ethanol swabs. This protocol was approved by the Emory University IACUC.

For the mobile mode of microdermabrasion, two vacuum pressure settings of 25 kPa and 50 kPa were tested; the 25 kPa setting was operated at 100, 200 and 300 passes and the 50 kPa setting was operated at 10, 30, 50, 80 and 100 passes. To perform microdermabrasion in triplicate, three monkeys were assigned for each pressure level group. One pass is defined as the movement of the microdermabrasion tip from one end to the other on the treated skin site exposed through the stencil slit. The hand-piece was manually moved at a speed of approximately 40 mm/s and the flow rate of microparticles was kept at 70% of the maximum flow rate of the instrument. The vacuum pressure of 50 kPa was selected because it is considered a medium microdermabrasion setting according to manufacturer specifications, and in preliminary experiments on porcine cadaver skin this pressure resulted in removal of full-thickness of stratum corneum (data not shown). The other pressure of 25 kPa was selected because we wanted to identify the effect at a lower suction pressure. A non-microdermabraded, but trimmed and ethanol-cleaned section of skin from the back of the monkeys was used as a negative control.

The stationary mode of microdermabrasion was performed by keeping the hand-piece stationary on the skin and exposing the skin to a vacuum pressure of 30 kPa or 50 kPa for 3 s or 6 s each. The conditions were tested in triplicate by performing microdermabrasion at each condition on three monkeys.

To facilitate direct comparison between microdermabrasion in the mobile mode and the stationary mode, the “effective” microdermabrasion exposure time in the mobile mode was calculated by dividing the tip diameter (7 mm) by the speed of tip movement (40 mm/s) and then multiplying by the number of passes.

A 6 mm skin biopsy was obtained from the center of each microdermabraded and control skin site (mobile mode = center of stencil; stationary mode = center of treated skin), mounted in OCT (optimal