Laser Treatment in Early Wound Healing and the Clinical Effect on Scar Formation

Katrine Elisabeth Karmisholt, MD
Department of Dermatology, Bispebjerg University Hospital, Copenhagen, Denmark. E-mail: katrine.karmisholt@gmail.com

Katrine Elisabeth Karmisholt defended her thesis in Faculty of Health and Medical Sciences, University of Copenhagen, Denmark on September 28, 2018. Principal Supervisor: Professor Merete Haedersdal, MD, PhD, DMSc, Bispebjerg University Hospital, Denmark. Chairman: Claus Zachariae, MD, DMSc, Gentofte University Hospital, Denmark. Co-supervisors: Professor Uwe Paasch, MD, Phd, University of Leipzig, Germany and Tonny Karlsmark, MD, DMSc, Bispebjerg University Hospital, Denmark. Assessment committee: Albert Wolkerstorfer, MD, PhD, University of Amsterdam, the Netherlands and Prof. Peter Bjerring, MD, PhD, DMSc, Moelholm Hospital, Vejle, Denmark.

The overall aim of this thesis was to investigate the potential clinical effects of laser treatment in early wound healing to reduce scar formation. Previously, *in vitro* and clinical studies have proposed that lasers intervention in inflammation-, proliferation- and remodeling phases of wound healing, may improve scar formation. However, no consensus regarding early laser treatment procedures to improve scar formation exists. In this thesis, a systematic review of the literature on early laser intervention to reduce scar formation was performed. Included studies were presented according to the wound healing phases in which the laser treatment was initiated (Study I). An experimental screening study was performed to investigate the importance of timing and fluence levels of a single exposure non-ablative fractional laser (NAFL, 1,540 nm) (Study II). Study II was performed on a full-thickness punch biopsy wound model in healthy volunteers with a randomized controlled intra-individual design. In Study III experimental testing of 3 repetitive 1,540 nm NAFL-treatments targeting all 3 wound healing phases was investigated in a randomized controlled split-wound trial on patients undergoing surgical excisions.


Claus Zachariae


Merete Hædersdal


Uwe Paasch


Tony Karlsmark


Peter Bjerring


Albert Wolkerstorfer

In the systematic review (Study I) a total of 25 trials were found eligible. The following lasers were applied: pulsed dye laser (PDL, 585/595 nm), potassium-titanyl-phosphate laser (KTP, 532 nm), diode laser (810 nm), NAFL (1,550 nm), fractional CO_2-laser (10,600 nm) and yttrium aluminum garnet (Er:YAG, 2940 nm) lasers. Four studies initiated laser intervention in inflammation phase and 3 of these studies found significant improvement on treated scars compared to untreated scars. Sixteen studies initiated laser treatment in the proliferation phase and 6 of these studies found significant improvement on laser treated scars compared to untreated control scars. In 5 studies laser treatment was initiated in remodulation phase and 2 studies found significant improvement on laser treated scars compared to untreated controls. The Cochrane Handbook 2011 Risk-of-Bias evaluation was adopted to evaluate the methodological quality of included trials. Based on these criteria a sufficient randomization procedure was provided in 4 studies and none of the included trials described allocation concealment. Low risk of bias was found with regard to blinding of outcome assessment as 15 studies provided a clear description

of outcome assessment blinding. Information on exclusion after randomization and loss to follow-up was provided in 16 studies. Higher quality studies are needed to fully confirm the impact of early laser treatment to reduce scar formation, but available evidence indicates that laser intervention applied in early wound healing phases holds potential to reduce scar formation.

In Study II, 16 healthy volunteers received a single NAFL-exposure in a standardized full-thickness punch biopsy wound model applied to buttocks area. NAFL-exposure one day before wounding, immediately after wounding or two weeks after wounding was tested at 3 fluence levels ranging from 30–70 mJ/mB, compared to untreated control wounds. Primary outcome was blinded on-site evaluation on Patient-Observer-Scar-Assessment-Scale (POSAS) with a total score ranging from 6–60 points (6 resembling normal skin and 60 worst imaginable scar) at 3 months follow-up. According to POSAS-total, and compared to untreated control scars, significant improvements were found on NAFL-treated scars with NAFL-exposure one day before wounding with medium-fluence (median difference 1, $p=0.03$), immediately after wounding with low-fluence (median difference 1.5, $p<0.05$), and two weeks after wounding with low-fluence (median difference 1, $p<0.05$). Differences between NAFL-treated and untreated control scars were sparse but study II showed that NAFL may improve scar formation at all 3 interventional time points and that low to medium fluences induce beneficial outcome.

In Study III, 32 patients received medium NAFL-fluence level (40–50 mJ/mB, fluence level determined from Study II) on excisional wounds, split and randomized to NAFL treatment versus untreated control. Treated wound halves received three NAFL-treatments sequentially targeting the inflammation-, proliferation-, and remodeling phases. Scars were evaluated at 3 months follow-up and primary outcome was on-site blinded evaluations according to POSAS-total. NAFL-treated scar halves appeared significantly improved compared to untreated control halves (NAFL-treated median 11 [range 9–12] vs control median 12 [range 10–16], $p<0.001$). Changes were subtle and covered a wide range of treatment response: in 63% NAFL-treated scar halves improved, in 26% no difference was detected and in 10% NAFL-treated scars rated worse than corresponding control.

In conclusion, the available body of evidence indicates that laser interventions applied during wound healing phases have the potential to improve scar formation. Experimental studies show promise for 1,540 nm NAFL exposure when applied prior to or in early wound healing to reduce scar formation. Furthermore, NAFL treatments as an integrated part of surgical procedures hold promise for improvement of scar formation

List of original publications

I. Karmisholt KE, Haerskjold A, Karlsmark T, Waibel J, Paasch U, Haedersdal M. Early laser intervention to reduce scar formation – a systematic review. J Eur Acad Dermatol Venereol 2018; 32: 1099–1110.

II. Karmisholt KE, Wenande E, Thaysen-Petersen D, Philipsen PA, Paasch U, Haedersdal M. Early intervention with non-ablative fractional laser to improve cutaneous scarring-A randomized controlled trial on the impact of intervention time and fluence levels. Lasers Surg Med 2018; 50: 28–36.

III. Karmisholt KE, Banzhaf CA, Glud M, Yeung K, Paasch U, Nast A, Haedersdal M. Laser treatments in early wound healing improve scar appearance: a randomized split-wound trial with nonablative fractional laser exposures vs. untreated controls.Br J Dermatol 2018; 179: 1307–1314.