

# Evaluation of delayed-type hypersensitivity (DTH) in healthy volunteers using innovative imaging techniques

M. Saghari<sup>1</sup>, P. Gal<sup>1</sup>, M.L. de Kam<sup>1</sup>, M.B.A. van Doorn<sup>2</sup>, J. Burggraaf<sup>1</sup>, M. Moerland<sup>1</sup>, R. Rissmann<sup>1</sup>

<sup>1</sup>Centre for Human Drug Research, Leiden, the Netherlands, <sup>2</sup>Department of Dermatology Erasmus Medical Centre, Rotterdam, the Netherlands

## Introduction

- Challenge models enabling direct pharmacodynamic assessment are necessary for development of immunomodulatory drugs.
- Keyhole limpet hemocyanin (KLH) is commonly used for studying T-cell dependent immune response.

## Aim

- To characterize the adaptive immune response after KLH immunization by measuring anti-KLH immunoglobulin (Ig) M and IgG titres
- To assess the skin response after intradermal administered KLH

## Methods

- Randomized, double-blind, placebo-controlled study
- 15 male healthy volunteers
- KLH (0.1 mg) or placebo immunization day 0 (4:1 ratio)
- KLH (0.001 mg) intradermal injection day 21 volar left forearm, untreated volar right forearm
- DTH assessment day 21 (pre-dosing) and day 23 (48h post-dosing) including Laser Speckle Contrast Imaging (LSCI), 2D and 3D photography, colorimetry, and visual erythema grading

## Results

- Treatments well-tolerated, no significant treatment related AEs
- Anti-KLH IgG and IgM titres significantly increased in KLH compared to placebo ( $p < 0.0001$  and  $p = 0.0014$ , respectively)
- Average redness values with Antera camera (figure 1) and basal flow with LSCI (figures 2 and 3) after intradermal KLH significantly increased in KLH immunization compared to placebo immunization and untreated right forearm

## Conclusions

- KLH administration well-tolerated
- KLH immunization induces quantifiable adaptive immune response
- LSCI and multispectral imaging following DTH assessment after intradermal KLH show potential to serve as novel objective, well-quantifiable assessments to study pharmacodynamic effects of immunomodulators

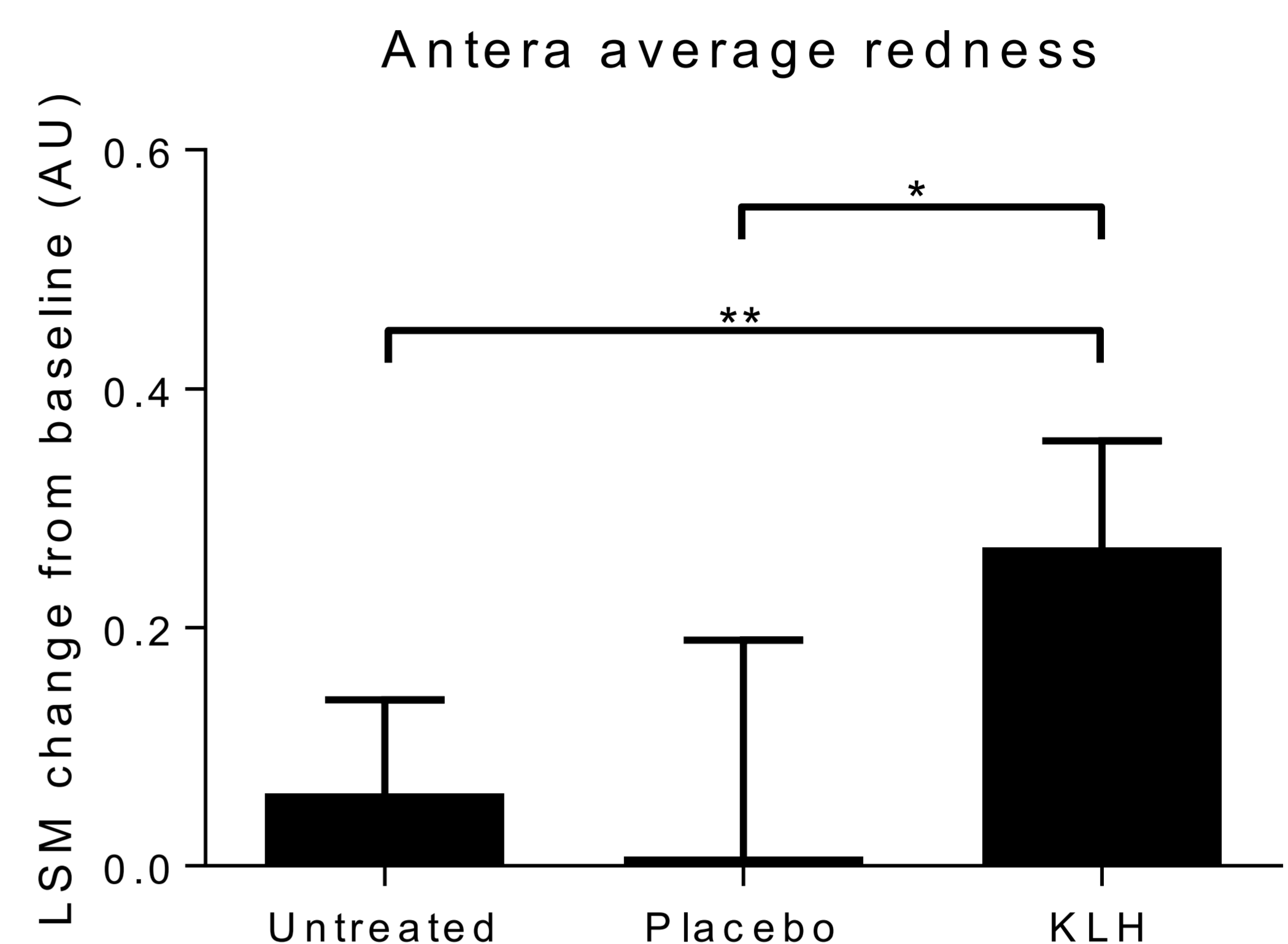


Figure 1: Least squares means (LSM) change from baseline (95% CI) antera average redness levels right forearm (untreated) and left forearm (placebo and KLH immunized groups). \* $p = 0.0172$ ; \*\* $p = 0.0019$  (AU, arbitrary unit)

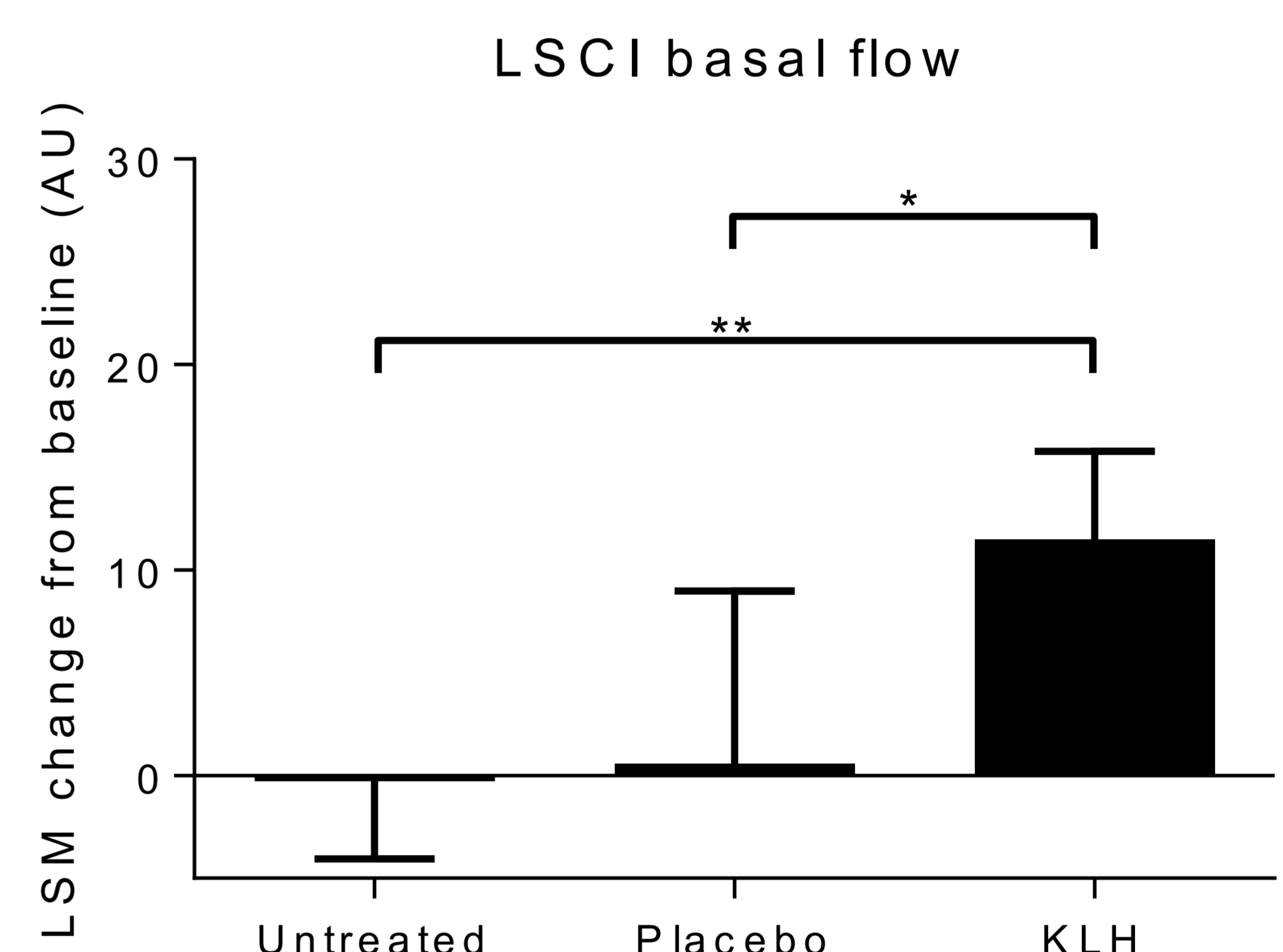


Figure 2: LSM change from baseline (95% CI) LSCI basal flow right forearm (untreated) and left forearm (placebo and KLH immunized groups). \* $p = 0.0263$ ; \*\* $p = 0.0002$  (AU, arbitrary unit)

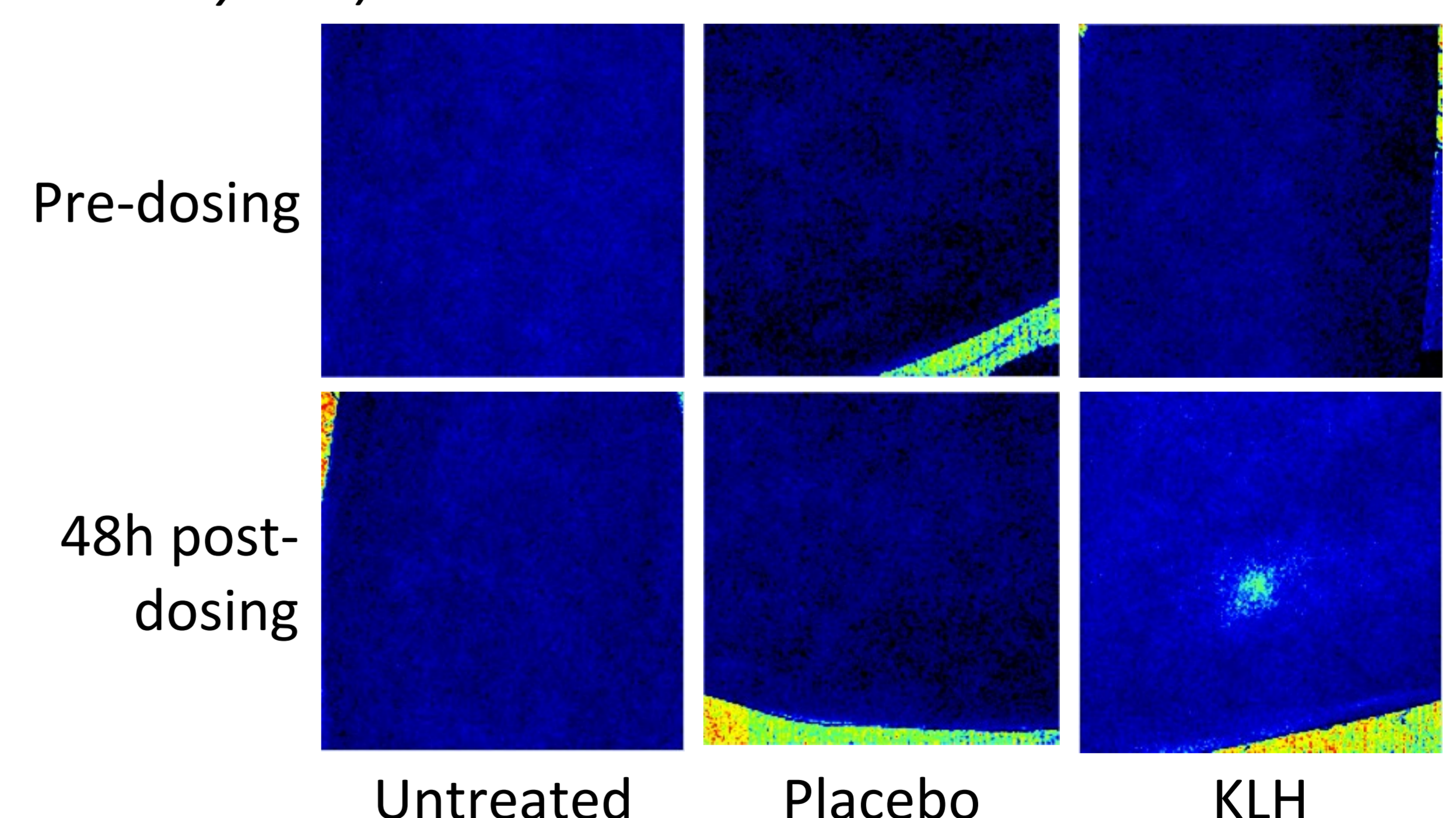


Figure 3: LSCI images right forearm (untreated) and left forearm (placebo and KLH immunized groups) before and after 48h of intradermal KLH administration