# A study of the methodology for determining Minimal Erythemic Dose for the UVB pain model

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## INTRODUCTION

The UVB (sunburn) model evokes inflammation of the skin by exposure to UVB radiation, thereby inducing inflammatory pain while also presenting some characteristics of chronic and neuropathic pain.

## AIM

The aim of the present study was to determine the most objective and sensitive method for determining the Minimal Erythemic Dose (MED) for subjects preceding UVB exposure when applying the UVB model for inflammatory pain in healthy human subjects.

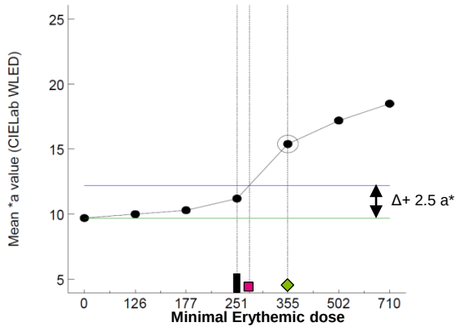
## METHODS

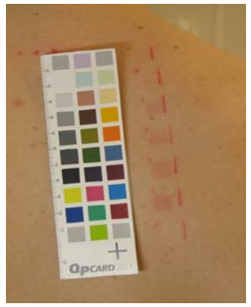
- 10 healthy subjects (5 males / 5 females).

- Application of 6 ascending doses (√2 increments) of UVB radiation, based on Fitzpatrick skin type. The third of the ascending doses was estimated to be the average MED for skin type, as described by **Sayre** et al.[1]

- 24 (±4) hours post-exposure erythema was assessed using the following methods:
  - **Visual inspection** performed by two raters on basis of consensus, in which MED is defined as the lowest dose required to induce a well-demarcated area of erythema;
  - **Calculation based on Colorimetric assessment** (a* of CIELAB) DSM II ColorMeter (Cortex Technology, Denmark), in which MED is defined as an increase of 2.5 a* unit from baseline, based on **Ferguson** et al.[2]
  - **Digital Image Analysis** (Erythemic Index / EI) in which a digital photograph taken in standardized lighting conditions was color-corrected (QP201 card and QP colorsoft 501 software) and analyzed for level of redness using ImageJ software.[3]

- Subjects were subsequently exposed to 3 MED.




Left: Individual graph of subject 3: The black line visualizes measured redness as a* value (dots). The **Sayre MED** (251 mJ/cm$^2$) is based on Fitzpatrick skin type. The green line represents the basal redness of the skin (a* value) and the blue line depicts the **Ferguson MED** (276 mJ/cm$^2$), defined as the Δ+ 2.5 a* from baseline and is marked with a magenta square. The **Visual MED** (355 mJ/cm$^2$) is marked with a green diamond.
Right: Photograph used for Digital Image Analysis. Color correction is performed by using the QP201 CARD and QP colorsoft 501 software.

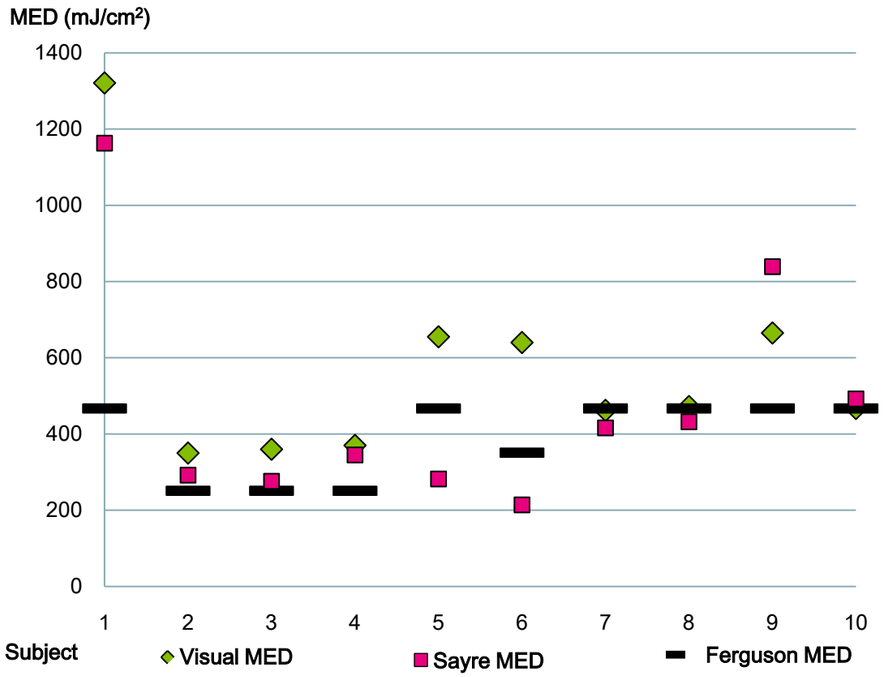
## RESULTS

All subjects had an MED within the dose range used, in all but one subject the visual determined MED resulted from the third or fourth highest UVB dose.

For all subjects the EI and a* values showed a comparable trend and the visually assessed value was always either one dose higher or lower than the Δ 2.5 a* value (blue line).

| Subject (skin type) | Estimated Sayre MED (mJ/cm$^2$) | Visual MED (mJ/cm$^2$) | Calculated Ferguson MED (mJ/cm$^2$) |
|---|---|---|---|
| 2 (II) | 251 | 355 | 292 |
| 3 (II) | 251 | 355 | 276 |
| 4 (II) | 251 | 355 | 345 |
| 6 (III) | 351 | 351 | 214 |
| 7 (IV) | 467 | 467 | 416 |
| 10 (IV) | 467 | 467 | 492 |
| 8 (IV) | 467 | 467 | 432 |
| 5 (IV) | 467 | 660 | 282 |
| 9 (IV) | 467 | 660 | 839 |
| 1 (IV) | 467 | 1321 | 1163 |

*Individual results of MED determination by comparing Visual MED and calculated Ferguson MED compared to estimated Sayre MED based on Fitzpatrick skin type.*




*Graphic overview of individual results of MED determination by Visual MED and calculated Ferguson MED compared to estimated Sayre MED based on Fitzpatrick skin type.*

## CONCLUSIONS

**Determination of an individual's Minimal Erythemic Dose (MED) is key element of the UVB model as it reduces inter-individual variability and thereby increases statistical power.**

The three methods were equally effective. As visual inspection is a quick and accurate way of determining the MED and was less error-prone than the colorimetric assessments or digital image analysis, we propose to use visual inspection for determination of MED in the UVB model.

## REFERENCES

1.Sayre et. al. Journal of the American Academy of Dermatology 1981;5:439-443.
2. Ferguson et al. Int. J. Cosmetic Science 1996. 18(5):203-18
3. Yamamoto et al. Skin Research and Technology 2008;14:26-34.



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