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Citation for published version (APA):

Felix Garza, Z. C., Liebmann, J., Born, M., Hilbers, P. A. J., & van Riel, N. A. W. (2018). *In silico clinical studies on the efficacy of blue light for treating psoriasis*. Poster session presented at 4th Dutch Bioinformatics & Systems Biology Conference, Lunteren, Netherlands.

Document status and date:

Published: 01/01/2018

Document Version:

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

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In silico clinical studies on the efficacy of blue light for treating psoriasis

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1. Introduction

The computational model for blue light irradiation of psoriatic skin (BLISS) ¹ reproduces the clinically observed average response to irradiation with blue light. However, it does not capture the inter-patient variability². It is essential that the model accounts not only for the average patient response but also the inter-patient variability. One approach to achieve this is to develop virtual patients (VPs), which are parameter sets that capture the variability in the real clinical investigation and sample the uncertainty in the model parameters ³. The VP sets included in the virtual population should account for the possible responses from perturbing the model and reflect the distribution of population-level data ⁴. The application of this methodology to BLISS would increase the confidence in the model predictions and enable the model to reflect the intersubject variability.

Here, a set of virtual patients is generated by fitting the distribution of the decrease in disease severity, referred to as change from baseline, after treatment with blue light from the clinical investigation of Pfaff *et al.* ² to the model BLISS. This virtual population is then used in a series of *in silico* clinical studies that explore whether the treatment response of psoriasis patients can be increased by modifying the settings used in the therapeutic protocol.

2. Approach

To generate the virtual patients from the model, the first step is to define the input parameters p that describe a VP and set the boundaries for these parameters. Then, an n number of plausible patients (PPs) are made using the Latin hypercube sampling method. From this plausible population, a PP is selected at random to run the model of blue light treatment for psoriasis. The virtual population is built by selecting the population with probability proportional to the prevalence in the real population relative to the prevalence in the plausible population.

The pool of virtual patients is used in a series of virtual clinical studies to assess whether the efficacy of blue light irradiation as treatment for psoriasis can be increased by using a combination of therapeutic settings different from the one currently used in the protocol of the clinical investigation ¹, i.e., fluence, length of treatment, and frequency of treatment sessions. Sets of simulations are implemented for these settings (Table 1).

Table 1. *In silico* clinical studies for therapeutic settings

No.	Tested parameter	Value
1	Fluence	15 - 500 Jcm ⁻²
2	Length of treatment	14 - 140 days
3	Frequency of treatment sessions	Daily, every other day, 2/3 as either daily or every other day treatment

3. Results

We generated a population of approximately 500,000 virtual patients that match the population-level characteristics of the patients in the clinical investigation. We analyzed the minimum number of virtual patients needed to obtain the same change from baseline distribution as in the clinical study of Pfaff *et al.* ². The minimum number of VPs was ~2,500 patients.

The results from the simulations performed with the virtual patients using different combinations of therapeutic settings suggest that the treatment efficacy can be increased for all patients, including those with low treatment response. This can be achieved by implementing a therapeutic protocol with daily treatment, and a higher fluence and length of treatment compared to the currently used settings.

4. Conclusion

This work enables the current model of blue light irradiation for psoriasis to reflect the inter-subject variability typically observed in clinical investigations and demonstrates the use of *in silico* clinical studies in the field of dermatology.

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