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Pulsed Dye Laser in psoriasis

A nerve-wrecking event?

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SCOPE OF THE THESIS

This thesis investigates the mechanisms and effects of Pulsed Dye Laser (PDL) therapy in the treatment of psoriasis, aiming to clarify the underlying mechanisms of PDL's therapeutic effects. The research encompasses a range of experimental approaches, including *in vitro*, *ex vivo*, *in silico*, and *in vivo* studies. The initial chapters focus on the impact of hyperthermia on various cell types, while the later chapters present clinical patient studies that explore the detailed morphology of the perivascular network in the skin and the changes it undergoes following PDL treatment. A more detailed overview of the chapters is provided below.

Chapter 1: Mechanisms of PDL Therapy in Psoriasis Remission

This chapter delves into the potential mechanisms by which PDL therapy induces long-term remission in psoriasis. It hypothesizes that PDL therapy targets perivascular nerves, leading to a disruption of neuro-inflammatory processes that contribute to psoriasis. The chapter reviews existing studies and proposes that repeated PDL treatments may cause nerve damage or reset neurogenic inflammation, thereby reducing T-cell activation and cytokine production, which are crucial in psoriasis pathogenesis.

Chapter 2: Thermal Sensitivity of Skin Cells to PDL Treatment

In this chapter, the focus shifts to the thermal effects of PDL treatment on different skin-relevant cells, including endothelial cells, smooth muscle cells, neuronal cells, and keratinocytes. The study investigates cell-specific responses to short-term hyperthermia (2-30 seconds) and shows that neuronal cells and keratinocytes are significantly more susceptible to thermal damage. Suggesting that PDL treatment may inflict damage to these cells, which could alter the neuro-inflammatory pathways in psoriasis.

Chapter 3: Functional Impact of PDL-Induced Hyperthermia on Blood Vessels

This chapter investigates the effects of moderate hyperthermia on the functionality of blood vessels, with a particular focus on endothelial cells, smooth muscle cells, and vascular nerves. The study utilizes isolated blood vessels in a wire-myograph setup exposed to controlled temperatures and reveals that hyperthermia impairs the functionality of these cell types to a similar extent. This finding contrasts with the cell-type-specific thermal sensitivity observed *in vitro* in Chapter 2, suggesting that during PDL treatment, it is unlikely that perivascular nerve fibers can be selectively damaged without also affecting overall vascular function.

Chapter 4: Correlation Between Clinical Assessment and Skin Anatomy in Psoriasis

Chapter 4 introduces patient-derived material, allowing us to study the baseline morphology and distribution of nerve fibers in the skin, particularly with regard to blood vessels. Here, the thesis investigates the correlation between clinical observations of psoriasis symptoms (such as erythema, induration, and scaling) and the underlying anatomical structures of the skin. By analyzing 3D microscopy images of psoriatic skin, the study finds partial alignment

between clinical assessments and histological features, highlighting the restrictions of current clinical evaluation methods in capturing the neuro-vascular anatomy of psoriasis lesions.

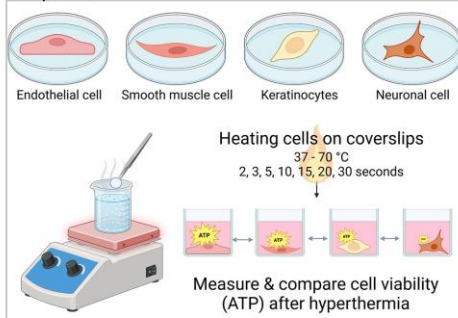
Chapter 5: Histological Changes in Psoriatic Skin Following PDL Treatment

In chapter 5 we explore histological changes in the skin of psoriasis patients before and after PDL treatment, with a focus on nerve fiber and blood vessel density. The study reveals that, while epidermal thickness decreases significantly in clinical responders, changes in nerve and vascular structures do not appear to correlate with treatment outcomes. These results suggest that the mechanisms underlying PDL-induced remission of psoriasis may involve factors beyond simple changes in skin anatomy, pointing to the need for further research into the functional aspects of nerve fibers and other potential mechanisms.

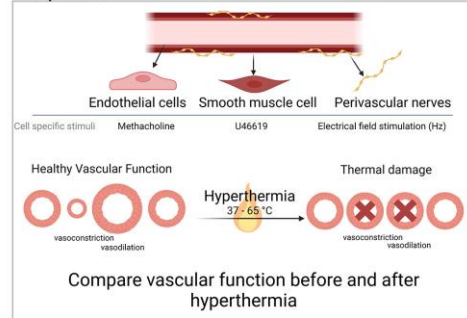
Chapter 6: General discussion

Chapter 6 summarizes the findings of our research and places them within a broader context. Additionally, it presents and discusses new questions and hypotheses that have emerged from the data.

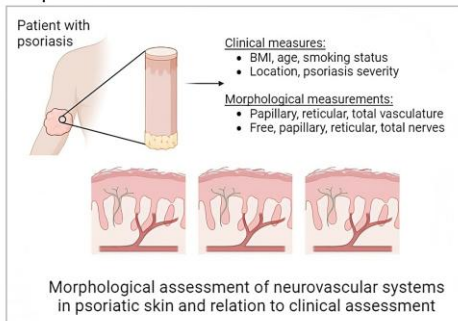
Chapter 2



Chapter 3



Chapter 4



Chapter 5

