

# SkinStim



# TABLE OF CONTENTS



**Product Overview..... Pg. 3**

**First and Second-Generation Products ..... Pg. 4**

**Targeted Proteins..... Pg. 5**

**Preclinical..... Pg. 6-7**

**Clinical..... Pg. 8-32**

**Target Protein Description.....Pg. 33**

**References.....Pg. 34-35**

# Product Overview

## SkinStim

SkinStim is a non-invasive portable bioelectric stimulation system designed for at-home use. An easy-to-use skin mask delivers proprietary low-intensity, low-frequency bioelectric signals to treat common skin conditions including age-related changes and acne.



**SkinStim's multi-patented technology modulates the gene expression** of key pro-regenerative skin proteins that naturally deplete with age. The system is designed to recruit stem cells, improve blood flow, and increase target proteins that contribute to skin elasticity, cellular repair, skin texture improvement, collagen production, and wrinkle reduction.



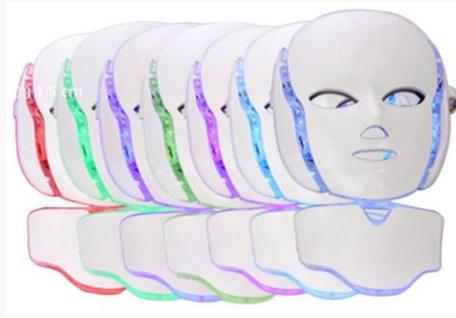
# Generation One

## Standard \$199- Bioelectric Stimulator



FDA clearance for at home use pending

## Premium \$399- Bioelectric Stimulator and LED Mask



FDA cleared

Click to add text

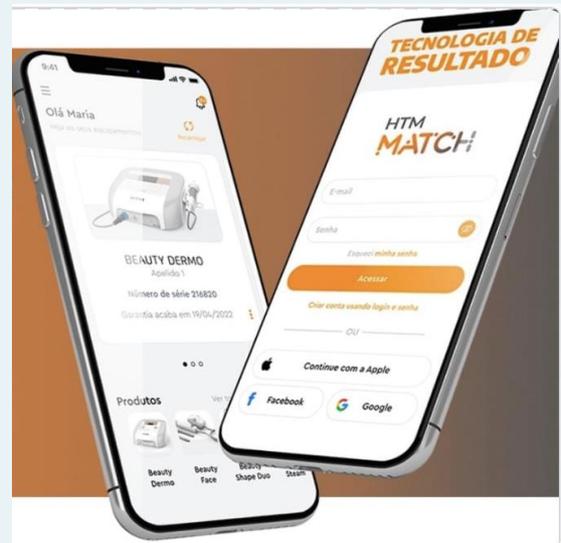


FDA clearance for at home use pending

# Generation Two

## Deluxe \$599

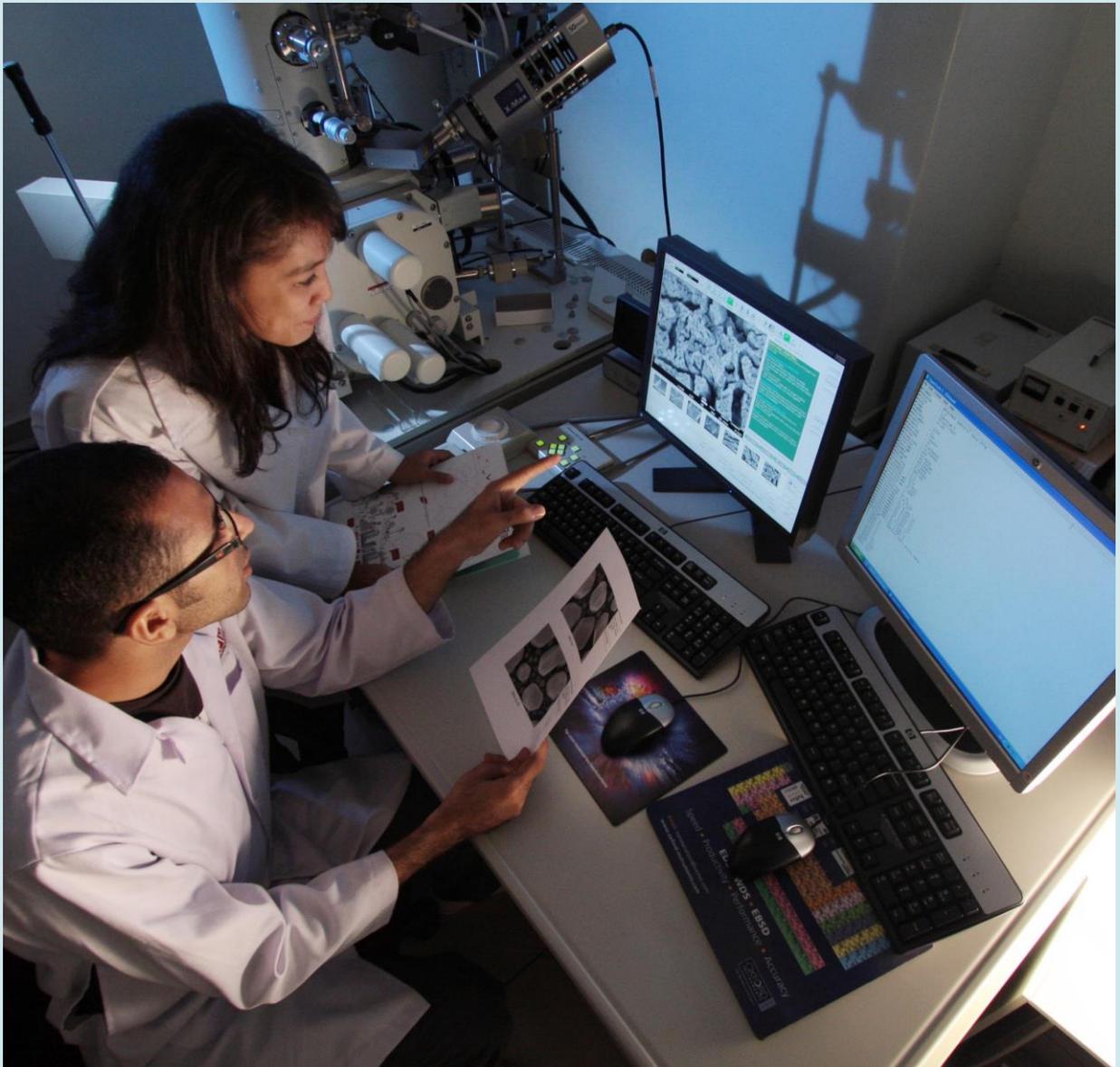
- Bioelectric/LED mask analyzes skin using artificial intelligence
- Provides customized treatment based on skin analysis
- Capable of connectivity via an app where customers can buy and download new signals
- The app option avoids tech waste for customers that can connect a mask through Bluetooth



# Target Proteins

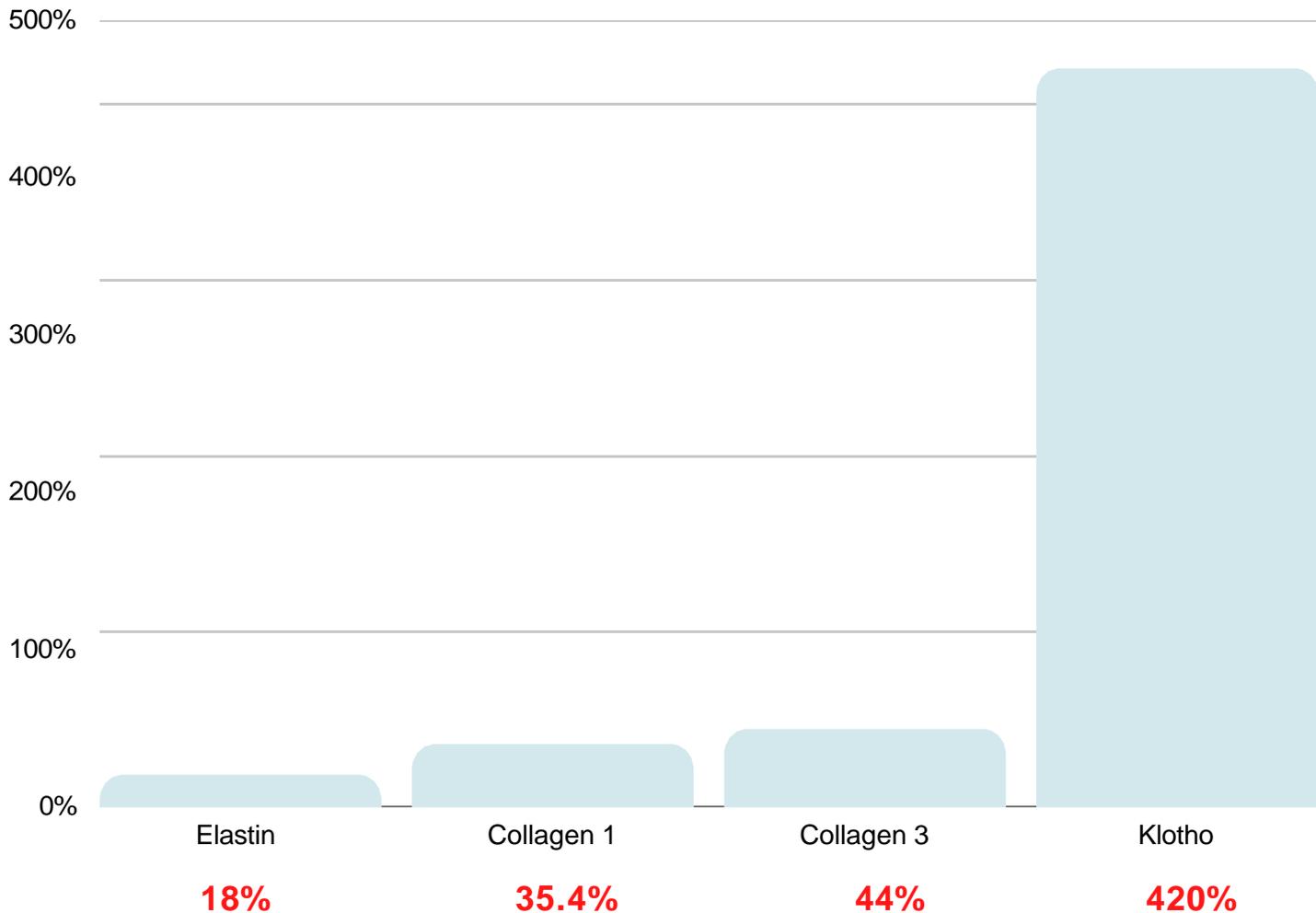
<b>Protein</b>	<b>Action</b>
Stromal Cell-Derived Factor 1 (SDF1) and Platelet-Derived Growth Factor (PDGF)	Stem cell homing and cell proliferation
Col17A, Collagen 1, and Collagen	Maintenance of skin structure and regulation of local stem cells
Tropoelastin/Elastin	Skin elasticity
Klotho	Anti-aging and DNA repair effects
Follistatin	General metabolic condition and anti-aging effects

# PRECLINICAL



# THREE DAY STIMULATION

★ No Animal Testing



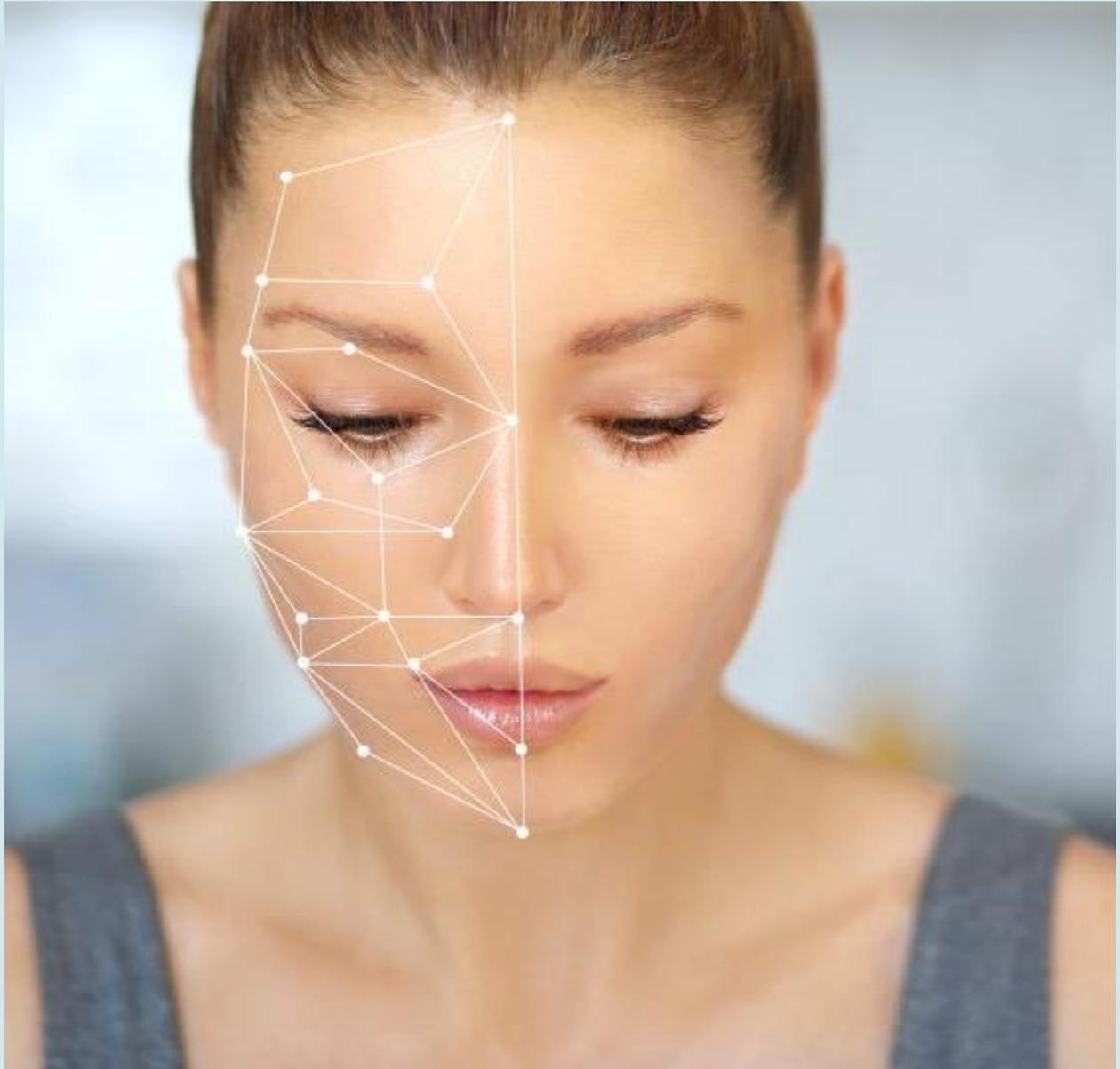
## Purpose:

The purpose of this research was to determine the bioelectric signaling sequence that produces the largest expression of Elastin, Collagen 1, Collagen 3, and Klotho.

## Methodology:

Human skin cells were stimulated *in vitro* for 60 minutes with an FDA-approved stimulator for three days. mRNA expression was analyzed in the cells for each target protein using RT-qPCR.

# CLINICAL



# A104 Skin Analyzer

The A104 Skin Analyzer is a photographic imaging tool that provides clinical measurement of surface and subsurface facial skin conditions. It measures ten dermal and epidermal skin parameters including pores, dark spots, wrinkles, texture, porphyrin, pigmentation, moisture, sensitive areas, brown areas, and sun damage.



The analyzer uses RGB visible light, PL polarized light, and UV ultraviolet light to measure skin conditions. The RGB white light detects pores, dark spots, and wrinkles. The PL light is polarized and detects surface texture, fine lines, wrinkles, and skin smoothness. The UV light detects skin irregularities including sun damage, acne, deep pigmentation, stain distribution, pore blockage, and oil secretion.

## Results Nomenclature

The results are expressed as percentages that compare the person's skin health to that of a group of same-age people. **The higher the percentage, the better the skin health for all parameters.**

**RGB Pore** detects circular surface openings of sweat glands. The percentage of pores measures the state of surface pores. A greater number of spots indicates severe plugging of pores. The measurement of pores is expressed in two colors; peach pink indicates small pores, and red indicates larger pores.

**RGB Spot** detects facial skin pigmentation, spot color, and size. Brown or red skin marks are distinguishable by the distinct color and contrast from the background skin tone. Spots vary in size and shape and are generally visible to the naked eye. The red line marks the dark area, and the green line marks the lighter areas.

# A 104 Skin Analyzer

## Results Nomenclature

**RGB Wrinkles** indicates the current state of lines on the skin caused by aging, dry skin, or expression lines. Wrinkles also indicates the existing skin texture and loss of collagen.

**PL Texture** indicates non-smooth areas of the skin. This can include lumps, patches, and irregularities caused by wrinkles, pits, scarring, sun and wind damage.

**UV Porphyrin** indicates blocked pores. It analyzes acne, closed acne, blackheads, oil secretion, and water and oil imbalance. It also indicates the secretion of oil and blackheads in the deep layers of the skin. Typically, the more sebum secretion, the greater the degree of acne in the epidermis. Red represents the more obvious acne, and pink represents the less obvious acne.

**UV Pigmentation** is the aggregation of skin pigmentation in the dermis. It refers to the discoloration in the deep skin. This is usually caused by an excessive use of cosmetics containing lead and mercury or too many chemical compositions. The red line indicates the darker color pigments, and the green color indicates the lighter color pigments.

**UV Moisture** indicates the status of skin hydration, especially in the deep skin.

**Sensitive Areas** indicates areas of inflammation and the degree of inflammation. The green circles indicate sensitive areas and the distribution of inflammation. It can also indicate a damaged part of the stratum corneum. Red represents a severely inflamed area.

**Brown Areas** shows skin metabolism, cellular activity, and the ability to repair of the skin dermis. For example, poor cellular activity can cause poor skin metabolism which can lead to poor repair capacity, inflammation and skin sensitivity. Poor metabolism can also affect water and oil distribution, increasing the risk of acne and wrinkles. Red lines represent areas of weak metabolism and green lines indicate areas where cellular activity is better.

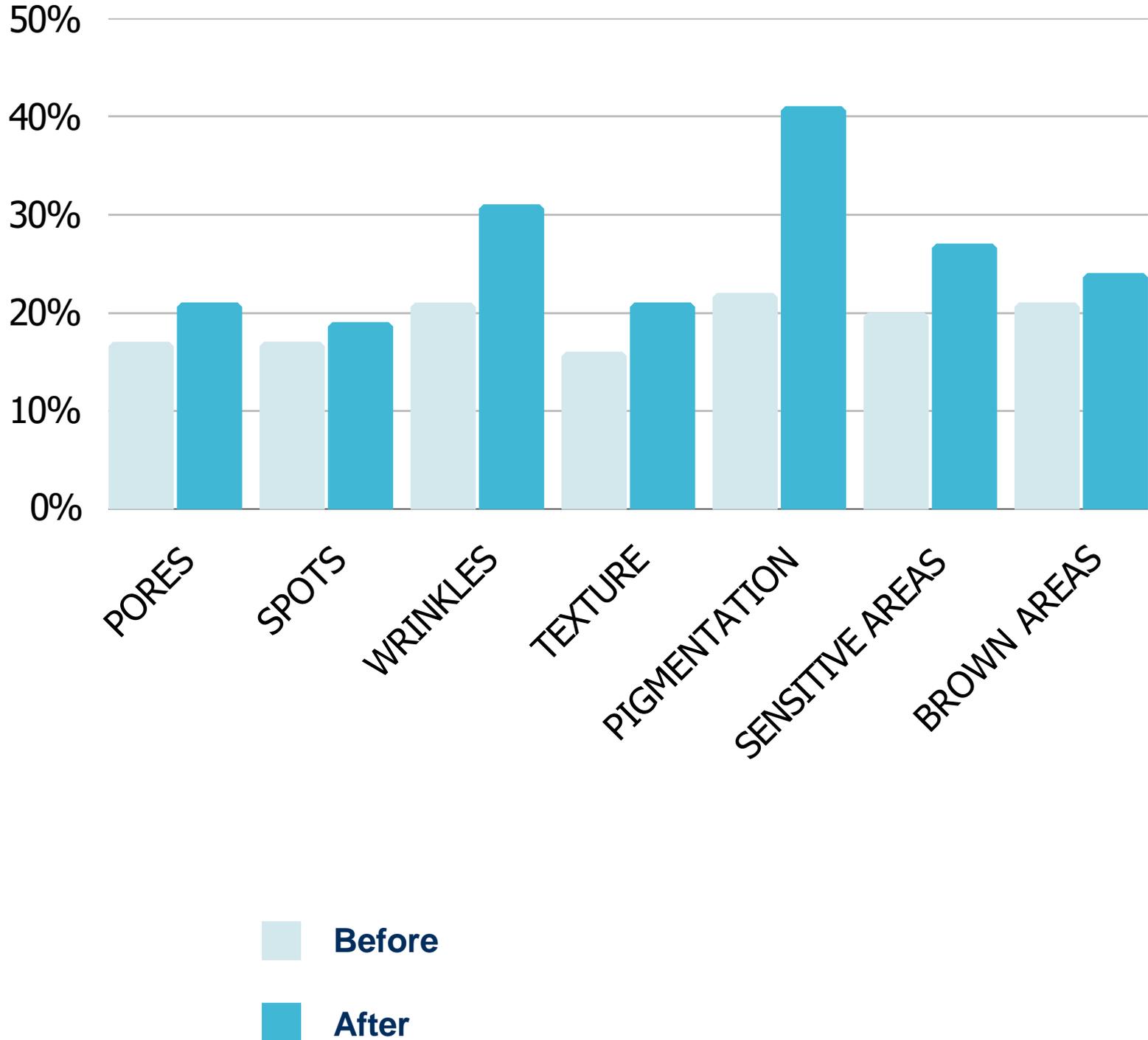
**UV Damage** indicates skin damage caused by ultraviolet rays. The red lines and spots represent more severe UV damage, and the green lines and spots represent the less severe UV damage.

# Case Study One

## 51-year-old Female

Three, 45-minute treatments per week for two weeks

### Before and After Two Week Treatment



The higher the percentage, the better the skin condition

# Case Study One

51-year-old Female

Before and After Two Week Treatment



**Before**



**After**

# Case Study One

Before and After Two Week Treatment  
RGB Spot



**Before**

17.4%

**After**

19.8%

# Case Study One

## Before and After Two Week Treatment RGB Wrinkle

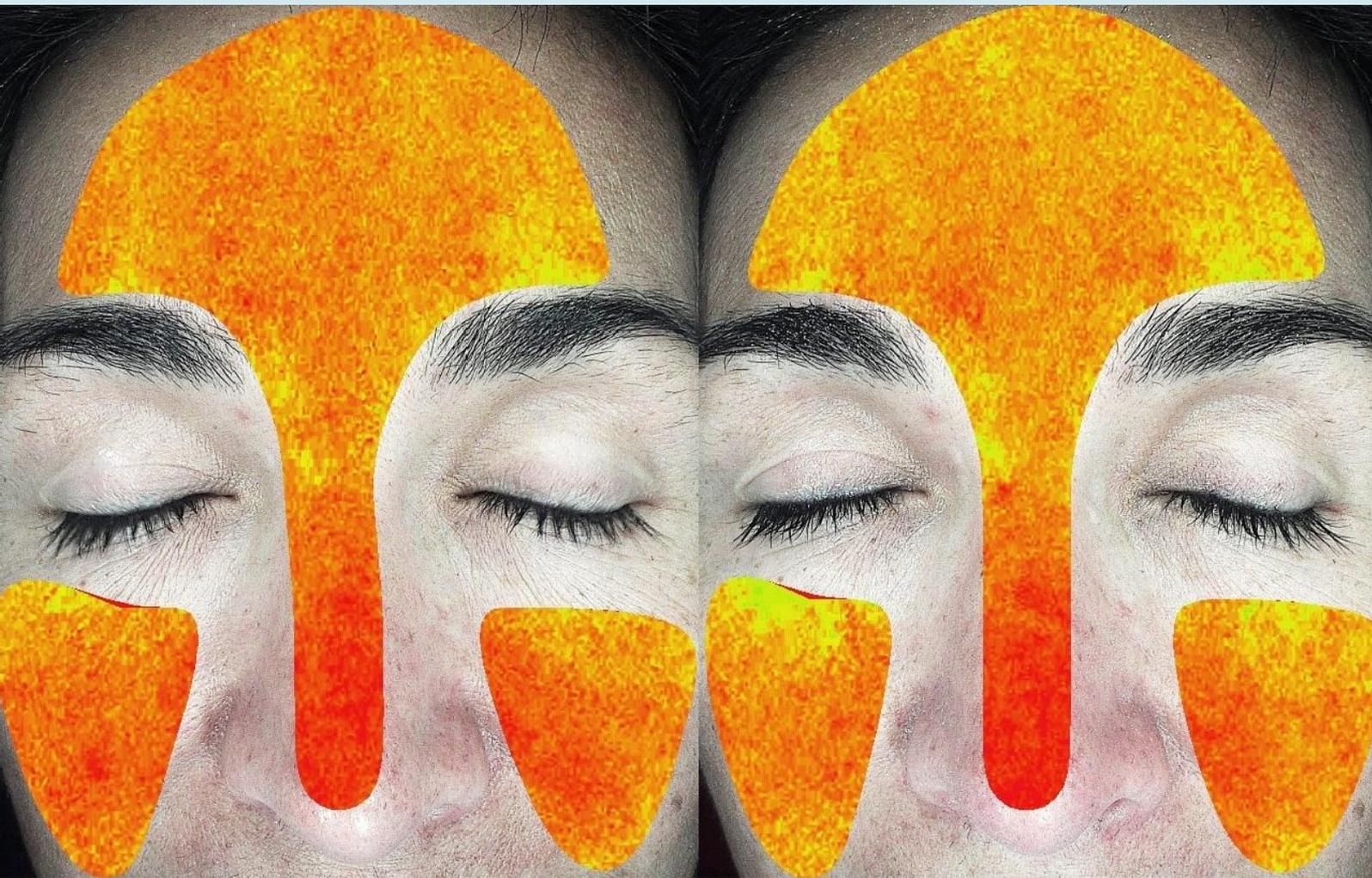


**Before**  
21.6%

**After**  
31.1%

# Case Study One

Before and After Two Week Treatment  
PL Texture



**Before**

16.3%

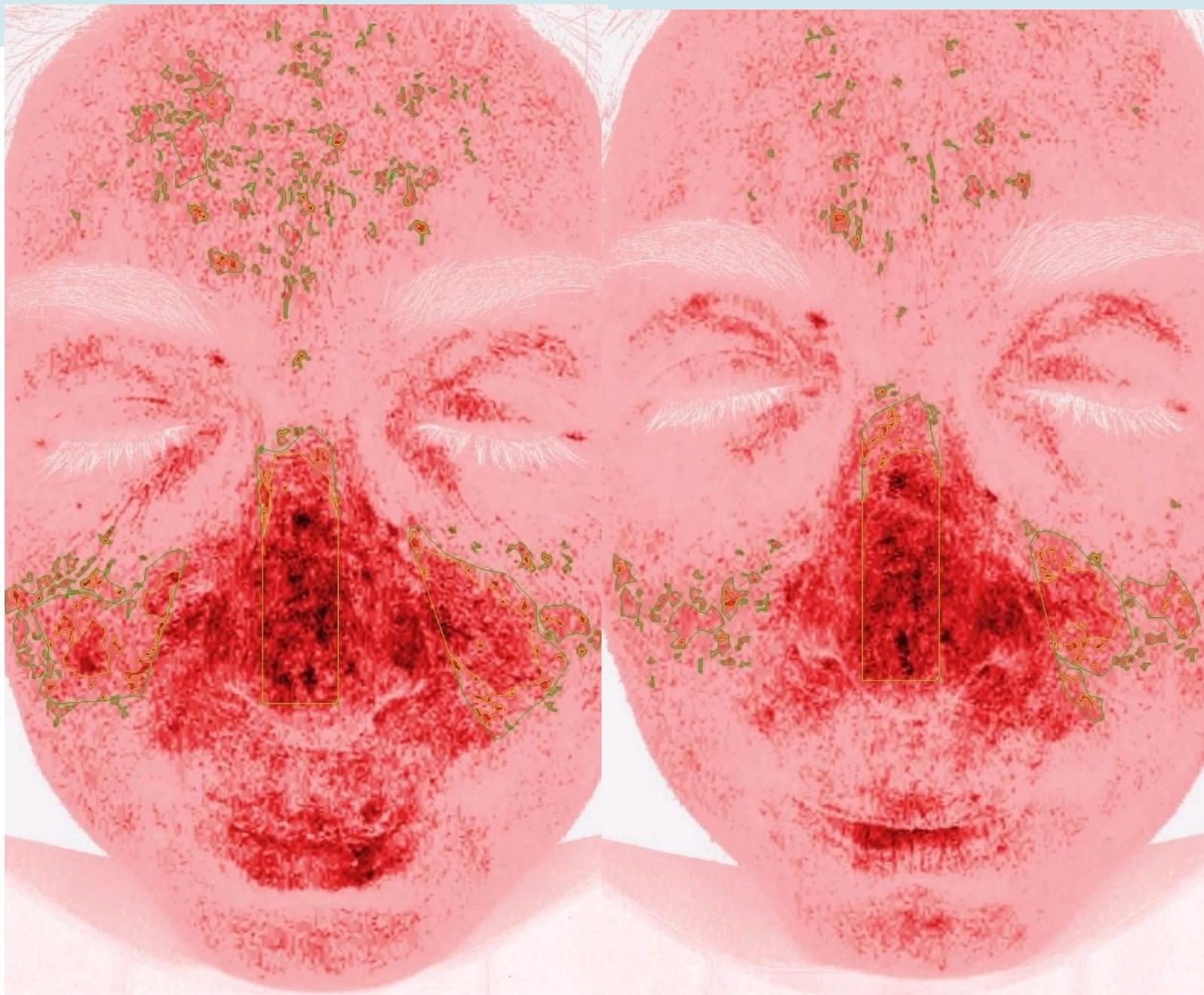
**After**

21.4%

-  Severe
-  Moderate
-  Mild

# Case Study One

## Before and After Two Week Treatment Sensitive Areas



**Before**  
20.2%

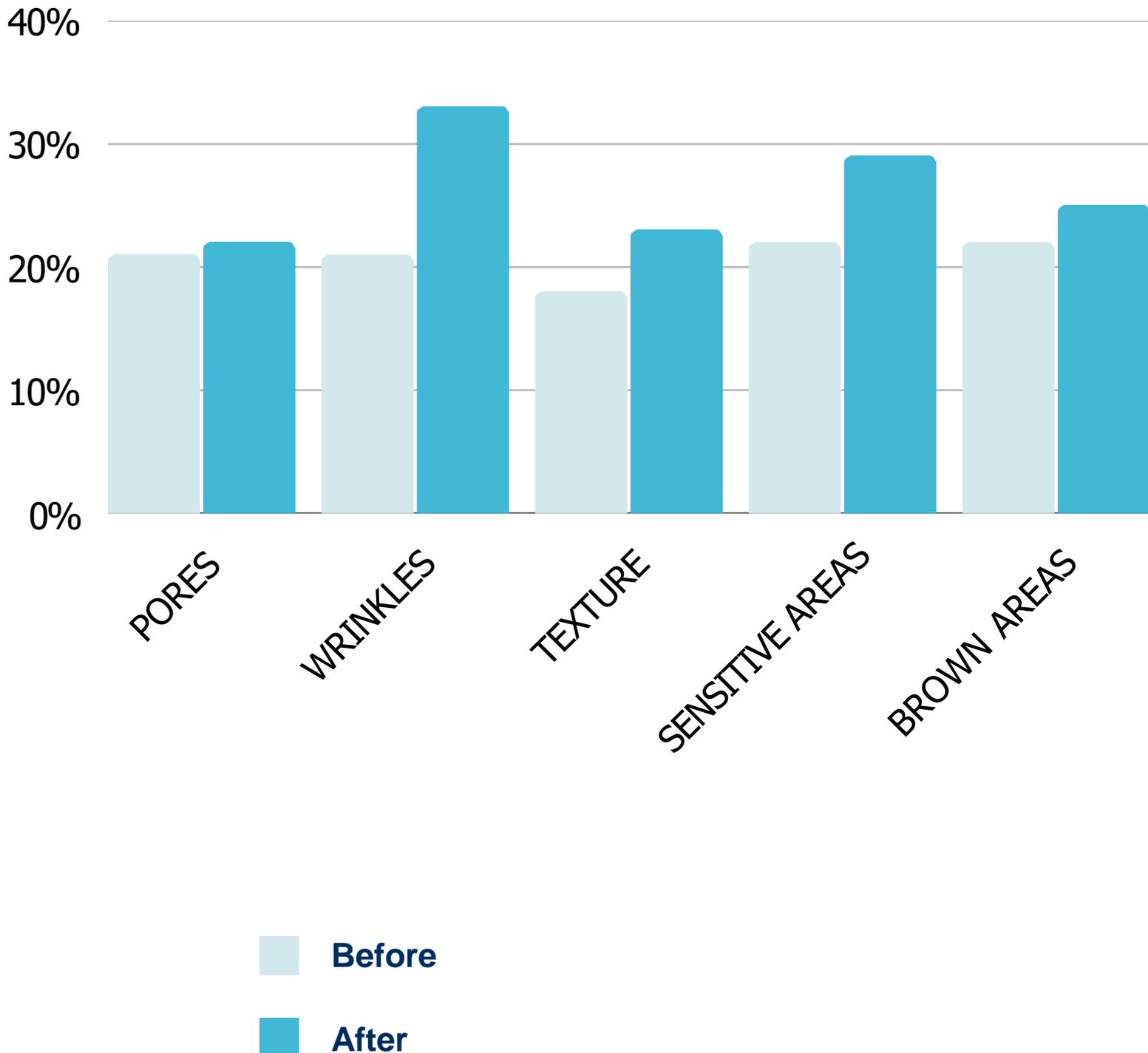
**After**  
27.4%

# Case Study Two

60-year-old Female

Three, 45-minute treatments per week for four weeks

**Before and After Four Week Treatment**



The higher the percentage, the better the skin condition

# Case Study Two

60-year-old Female

Before and After Four Week Treatment



**Before**



**After**

# Case Study One

## Before and After Four Week Treatment RGB Wrinkle



**Before**  
21%



**After**  
33%

# Case Study Two

## Before and After One Month Treatment PL Texture



**Before**

18%

**After**

23%

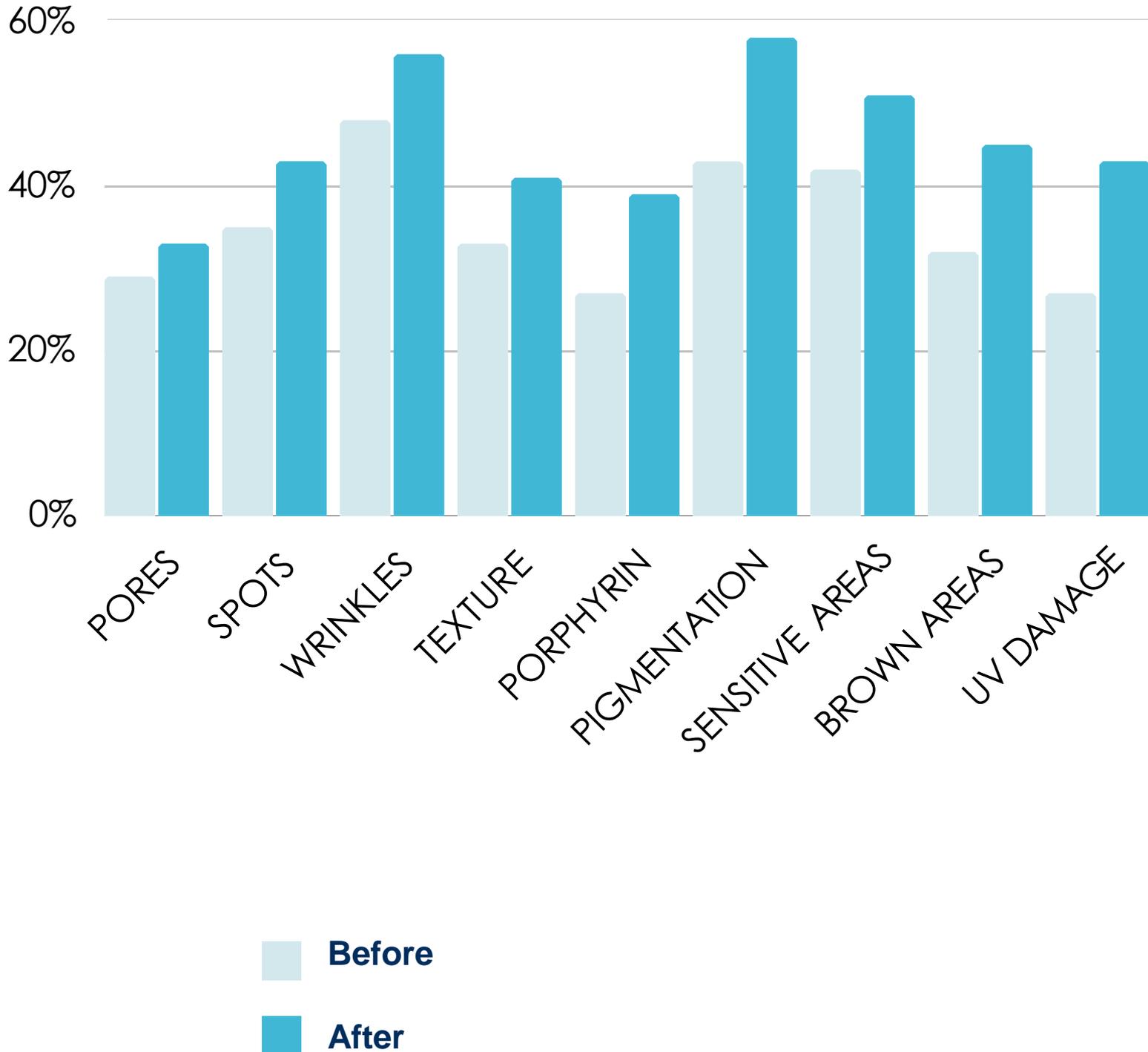
-  Severe
-  Moderate
-  Mild

# Case Study Three

Female, Age 23

Three, 45-minute treatments, per week for four weeks

## Before and After Four Week Treatment



The higher the percentage the better the skin condition

# Case Study Three

23-year-old Female

Before and After Four Week Treatment



**Before**

**After**

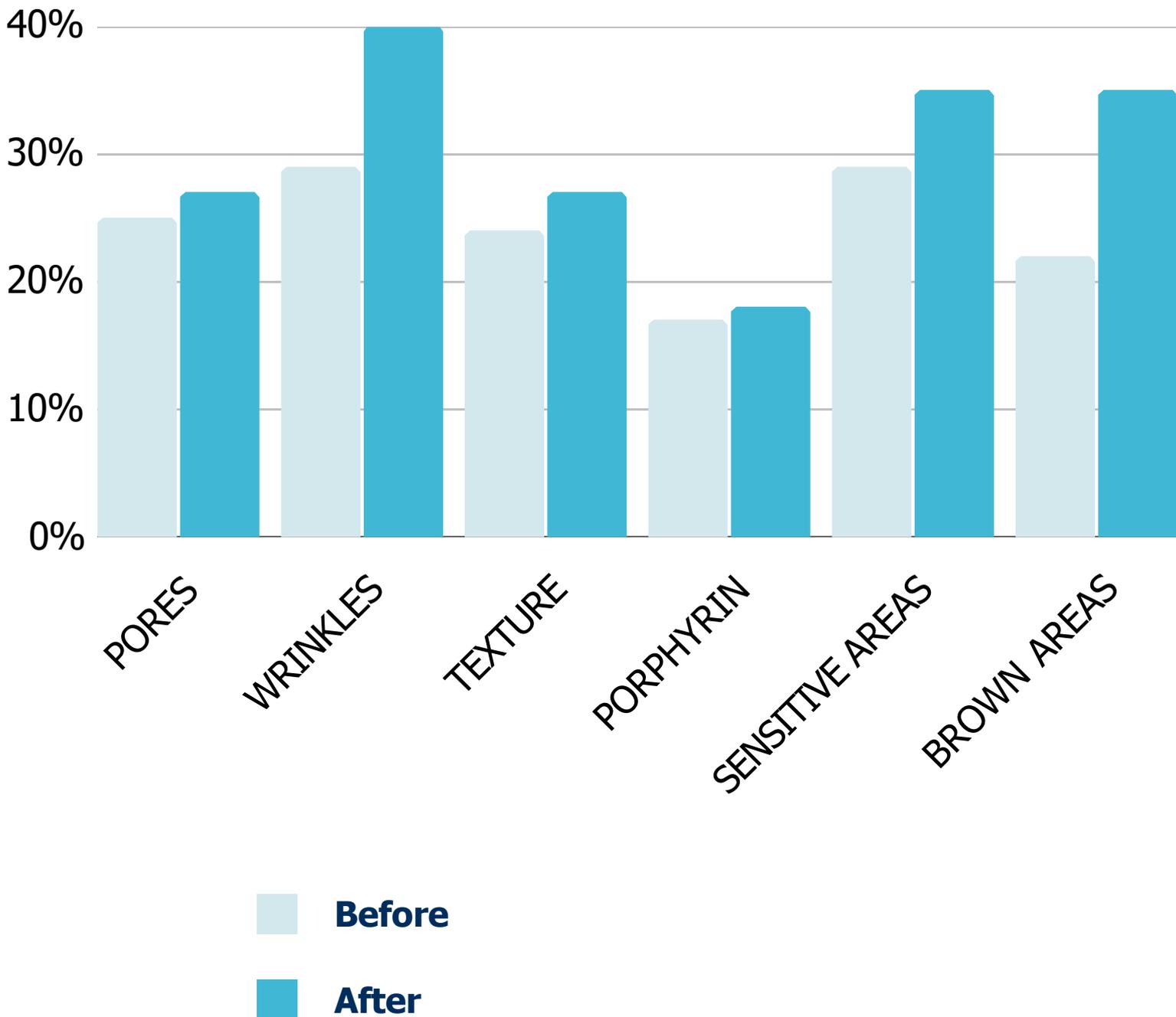
**Treated or Acne**

# Case Study Four

41-year-old Female

One 45-minute treatment per week for four weeks

## Before and After Four Week Treatment



The higher the percentage, the better the skin condition

# Case Study Four

41-year-old Female

Before and After Four Week Treatment



**Before**

**After**

# Case Study Four

## Before and After Four Week Treatment RGB Wrinkle



**Before**

29.8%

**After**

40.2%

# Case Study Four

## Before and After Four Week Treatment Sensitive Areas



**Before**  
29.8%



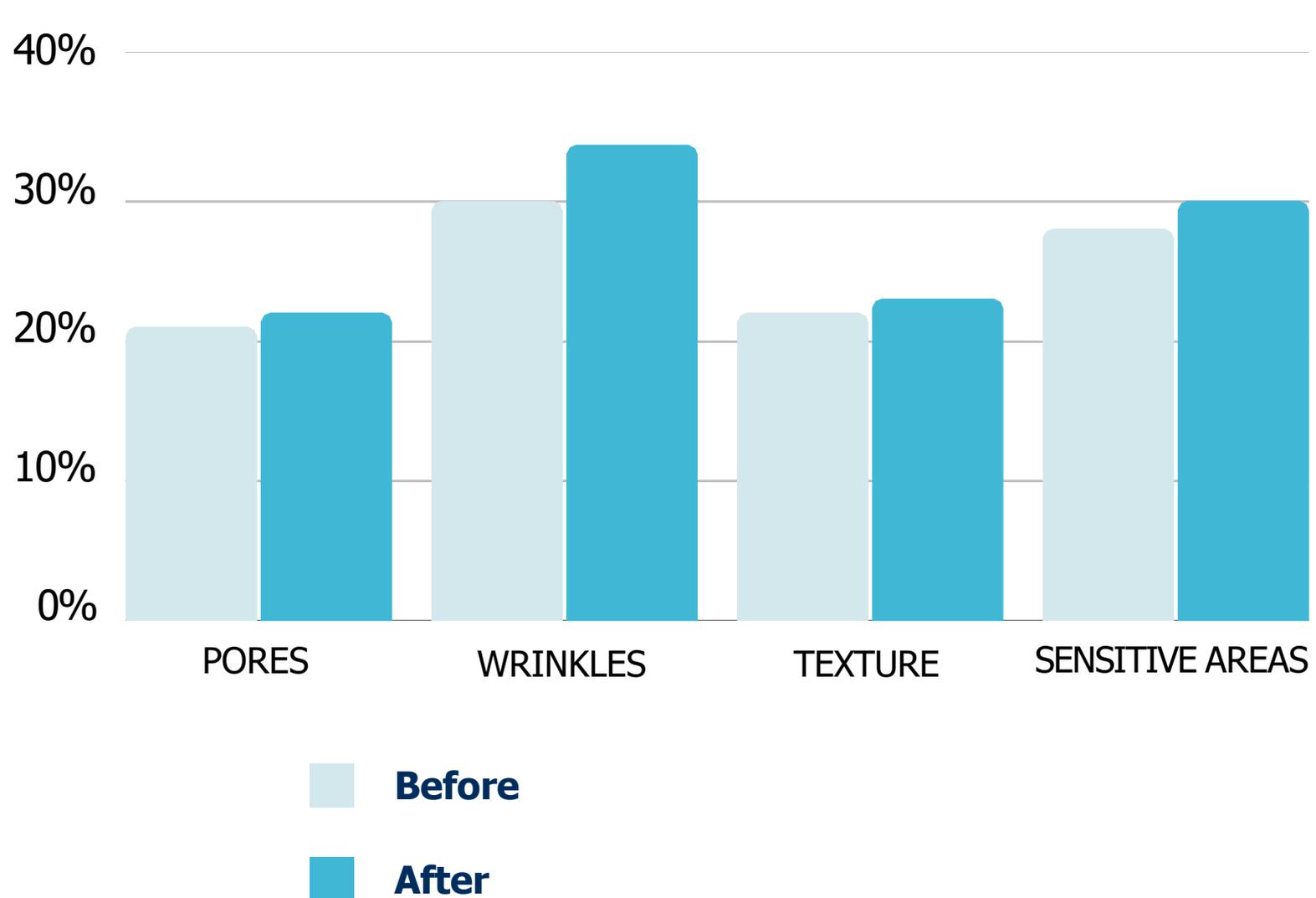
**After**  
35.1%

# Case Study Five

## 60-year-old Female

Three 45-minute treatments per week for four weeks

### Before and After Four Week Treatment



The higher the percentage, the better the skin condition

# Case Study Five

60-year-old Female

Before and After Four Week Treatment



Before

After

# Case Study Four

## Before and After Four Week Treatment RGB Wrinkle



**Before**  
30.7%

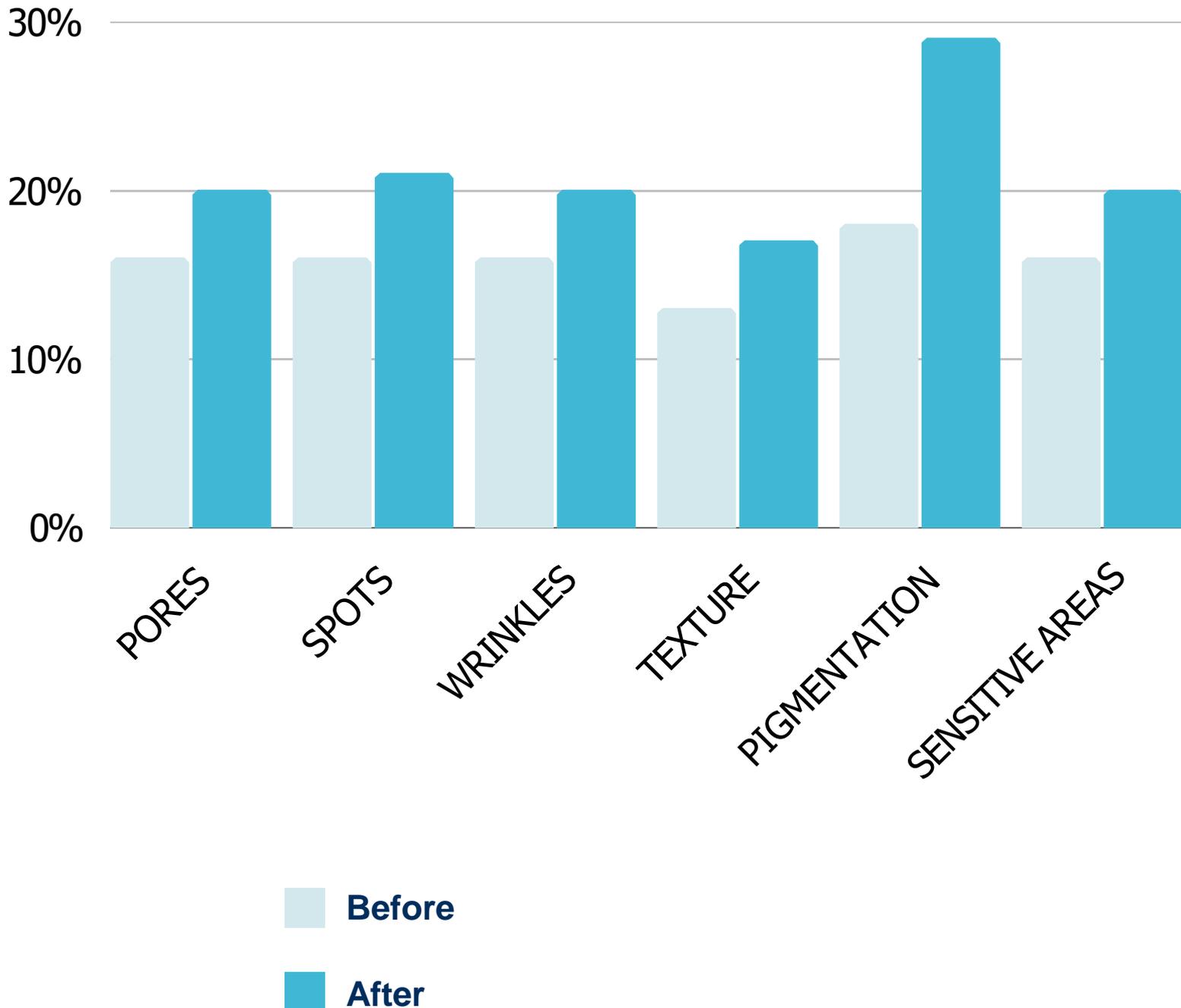
**After**  
34.2%

# Case Study Six

61-year-old Female

Three 45-minute treatments per week for two weeks

**Before and After Two Week Treatment**



★ The higher the percentage, the better the skin condition

# Case Study Six

61-year-old Female

Before and After Two Week Treatment



Before



After

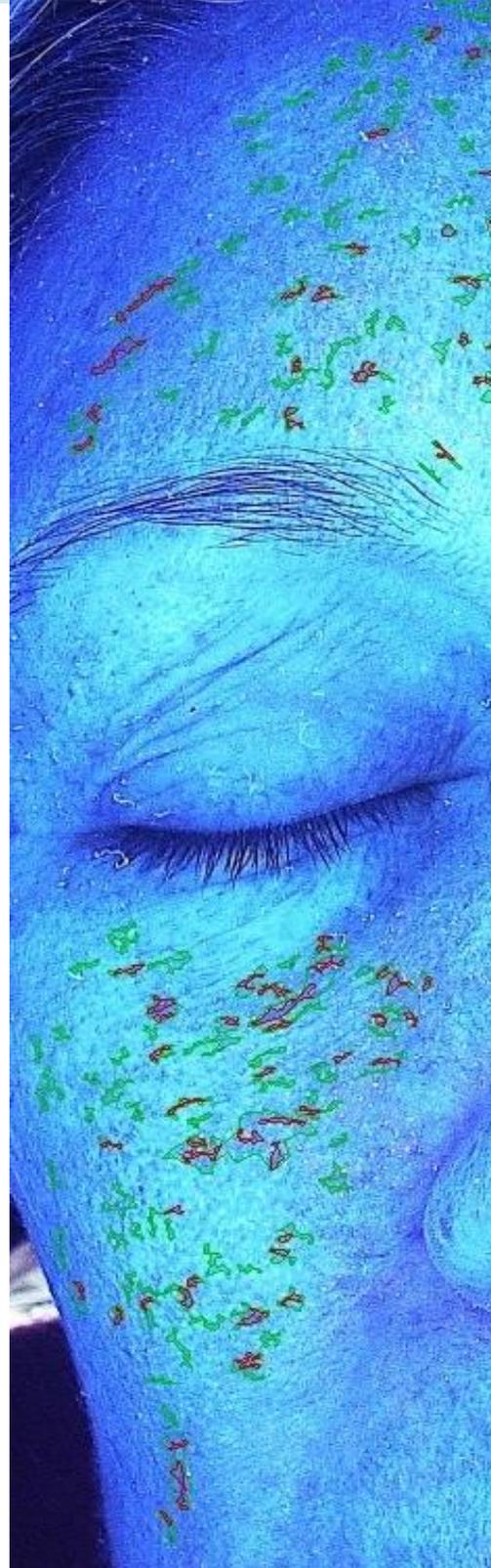
# Case Study One

## Before and After Two Week Treatment UV Pigmentation

**Before**  
18%



**After**  
29%



# Target Proteins

## Mesenchymal Stem Cells (MSCs)

Mesenchymal stem cells are self-renewing cells from fat and bone marrow that can differentiate into various cell lineages [10, 11].

## SDF 1A

The stromal cell-derived factor 1 $\alpha$  (SDF1) proprietary signal recruits MSCs to the area where the bioelectric signal is applied [1, 2, 3]. The upregulation of SDF1 mobilizes and recruits MSCs from bone marrow to proper locations to repair damaged tissues [1, 2, 3, 4].

## PDGF

Platelet-derived growth factor (PDGF) is a family of proteins that mediates tissue remodeling [12, 13]. PDGF upregulated during the SkinStim treatment encourages healthy keratinocyte cell growth, migration, and re-epithelization for the MSCs recruited via the SDF1 proprietary signal [13].

## Collagen 17A1

Collagen (COL17A1) is a protein found in the dermo-epidermal membrane and regulates local stem cells [17].

## Collagen 3A1 and Collagen 1A1

COL1 and COL3 are proteins best for improving skin elasticity. It provides structural support to tissues and plays important roles in cellular processes.

## VEGF

Vascular endothelial growth factor (VEGF) is a protein essential in blood vessel formation and the inflammatory response. It also helps with recruiting MSCs [6, 7]. VEGF is therapeutic to enhance skin repair and regeneration through angiogenesis and recruitment of MSCs [3, 4, 8].

## Klotho

Klotho is a protein known for its anti-aging effects [18][19]. In the scientific field of aging, Klotho has gained significant interest due to its' correlation with disease and aging.

## Tropoelastin

Tropoelastin is the precursor protein for elastin, responsible for generating elastic fibers for tissue elasticity and resistance [21]. Defects in the elastin gene are seen in patients who exhibit loose, sagging skin [21, 22]. Increased elasticity improves skin tissue regeneration and angiogenesis.

## References

- 1 <https://www.sciencedirect.com/science/article/pii/S0022202X1536014>  
CXCR4 in Epidermal Keratinocytes: Crosstalk within the Skin
- 2 <https://ashpublications.org/blood/article/104/2/565/18334/Role-of-the-CXCR4-SDF-1-chemokine-axis-in> Role of the CXCR4/SDF-1 chemokine axis in circulating neutrophil homeostasis
- 3 <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0068972>  
miR-27b Represses Migration of Mouse MSCs to Burned Margins and Prolongs Wound Repair through Silencing SDF-1a
- 4 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4621221/>  
A new method of wound treatment: targeted therapy of skin wounds with reactive oxygen species- responsive nanoparticles containing SDF-1 $\alpha$
- 5 [https://onlinelibrary.wiley.com/doi/full/10.1002/bit.27601?casa\\_token=KY5q\\_VqxPVwAAAAA%3A4M7qymsN4kwuZ8HEnJPjrrR14Mqmn\\_P3lJfOoXNcaEw9lFuE-tgfF0Myrd0dqQWjama-zWL5SEF05tST](https://onlinelibrary.wiley.com/doi/full/10.1002/bit.27601?casa_token=KY5q_VqxPVwAAAAA%3A4M7qymsN4kwuZ8HEnJPjrrR14Mqmn_P3lJfOoXNcaEw9lFuE-tgfF0Myrd0dqQWjama-zWL5SEF05tST)  
SDF-1 $\alpha$  gene-activated collagen scaffold drives functional differentiation of human Schwann cells for wound healing applications
- 6 <https://genomebiology.biomedcentral.com/articles/10.1186/gb-2005-6-2-209>  
The vascular endothelial growth factor (VEGF) family: angiogenic factors in health and disease
- 7 <https://www.sciencedirect.com/science/article/pii/S0022202X15526328>  
Molecular Mechanisms of VEGF-A Action during Tissue Repair
- 8 <https://link.springer.com/article/10.1007/s00403-009-1018-7> Human skin-derived mesenchymal stem cells as a source of VEGF and nitric oxide
- 9 <https://www.ahajournals.org/doi/10.1161/01.CIR.0000124062.31102.57>  
Local Delivery of Marrow-Derived Stromal Cells Augments Collateral Perfusion Through Paracrine Mechanisms
- 10 [https://www.liebertpub.com/doi/full/10.1089/scd.2013.0567?casa\\_token=iGEb\\_KUXiX4AAAAA%3A1-H2L9XfxZ8WSc8PflB9-byfi8uzbl4UIG6-PIF01MVRnFgT1n4xsP-Bk2sS45mldN\\_ogRmoL1Y](https://www.liebertpub.com/doi/full/10.1089/scd.2013.0567?casa_token=iGEb_KUXiX4AAAAA%3A1-H2L9XfxZ8WSc8PflB9-byfi8uzbl4UIG6-PIF01MVRnFgT1n4xsP-Bk2sS45mldN_ogRmoL1Y) Mesenchymal Stem Cell Paracrine Activity Is Modulated by Platelet Lysate: Induction of an Inflammatory Response and Secretion of Factors Maintaining Macrophages in a Proinflammatory Phenotype
- 11 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7085399/>  
Paracrine Mechanisms of Mesenchymal Stromal Cells in Angiogenesis
- 12 <https://www.pnas.org/content/88/2/565.short>  
Injury induces in vivo expression of platelet-derived growth factor (PDGF) and PDGF receptor mRNAs in skin epithelial cells and PDGF mRNA in connective tissue fibroblasts

## References

- 13 <https://journals.sagepub.com/doi/full/10.3727/096368912X637064>  
Adipose Tissue-Derived Mesenchymal Cells Support Skin Reepithelialization through Secretion of KGF-1 and PDGF-BB: Comparison with Dermal Fibroblasts
- 14 <https://www.nature.com/articles/s41598-018-30404-x>  
Topical administration of EGF suppresses immune response and protects skin barrier in DNCB- induced atopic dermatitis in NC/Nga mice
- 15 [https://www.sciencedirect.com/science/article/pii/S0305417904000816?casa\\_token=w5znS6rlbK0AAAAA:d9mGIJRJBOUXNAX\\_73xBFt9fMGMcjllO1UWXTqD67yOBPRN1lSaDEamAhzsQ26ZNVbz7K\\_I93g](https://www.sciencedirect.com/science/article/pii/S0305417904000816?casa_token=w5znS6rlbK0AAAAA:d9mGIJRJBOUXNAX_73xBFt9fMGMcjllO1UWXTqD67yOBPRN1lSaDEamAhzsQ26ZNVbz7K_I93g)  
The healing-promoting effect of saliva on skin burn is mediated by epidermal growth factor (EGF): role of the neutrophils
- 16 [https://www.jidonline.org/article/S0022-202X\(15\)33917-8/fulltext](https://www.jidonline.org/article/S0022-202X(15)33917-8/fulltext)  
The Epidermal Growth Factor Receptor System in Skin Repair and Inflammation
- 17 <https://onlinelibrary.wiley.com/doi/full/10.1111/exd.13550>  
Life before and beyond blistering: The role of collagen XVII in epidermal physiology
- 18 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC417422/>  
Klotho Mice: A Novel Wound Model of Aged Skin
- 19 [https://www.sciencedirect.com/science/article/pii/S0006291X1630451X?casa\\_token=\\_5zgnMcWp38AAAAA:hITavHPK5nHNJWCbjYr2ntOQi3NErrwVaH2O7LruDkG\\_3717odAZKyDszzwAuo0YVbV7iefvLMk](https://www.sciencedirect.com/science/article/pii/S0006291X1630451X?casa_token=_5zgnMcWp38AAAAA:hITavHPK5nHNJWCbjYr2ntOQi3NErrwVaH2O7LruDkG_3717odAZKyDszzwAuo0YVbV7iefvLMk)  
Wound healing delays in  $\alpha$ -Klotho-deficient mice that have skin appearance similar to that in aged humans – Study of delayed wound healing mechanism
- 20 <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1524-475X.2008.00410.x>  
Growth factors and cytokines in wound healing
- 21 [https://www.sciencedirect.com/science/article/pii/S1357272508001453?casa\\_token=xKPj7GPSVdMAAAAA:oBCEYMI5ll45oAja7uwZ0CipRPeZyaK\\_p2kvc98Clwo ci7mXDy gnmCNJwScLCTi1bDLqOdWoztM](https://www.sciencedirect.com/science/article/pii/S1357272508001453?casa_token=xKPj7GPSVdMAAAAA:oBCEYMI5ll45oAja7uwZ0CipRPeZyaK_p2kvc98Clwo ci7mXDy gnmCNJwScLCTi1bDLqOdWoztM)
- 22 <https://www.sciencedirect.com/science/article/pii/S0022202X15422274>  
Ultraviolet Radiation Increases Tropoelastin Accumulation by a Post-Transcriptional Mechanism in Dermal Fibroblasts