Phototherapy

JURAJ HEGYI
FNUSA & MU

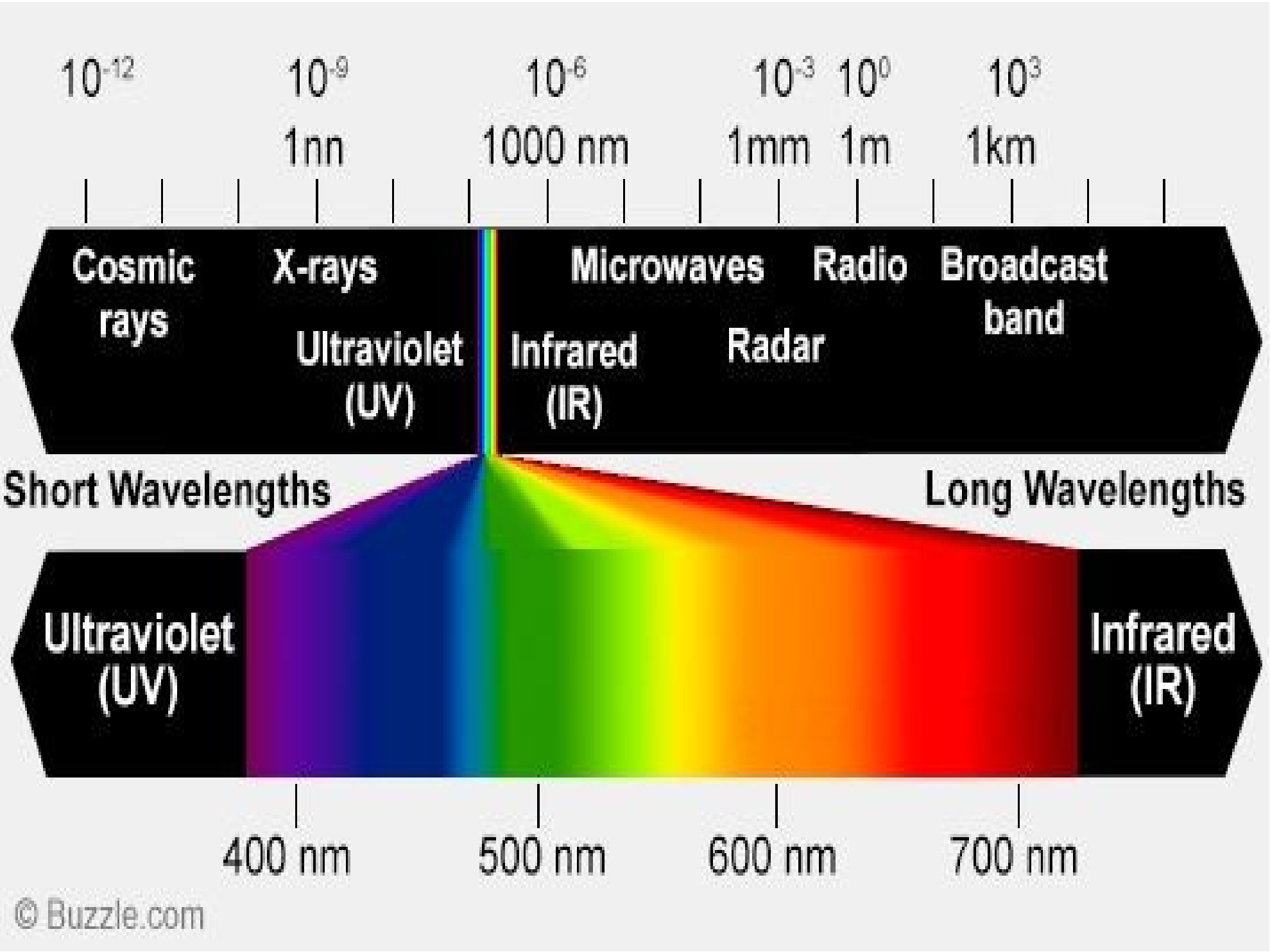
Definitions

- PHOTOTHERAPY: It is a form of treatment for skin conditions involving the administration of non ionizing radiation (most commonly within the ultraviolet part of the electromagnetic spectrum) in a controlled manner to the skin
- PHOTOBIOLOGY: It is the study of the effects of UV and VL on living matter
- PHOTODERMATOLOGY: It is the study of normal as well as abnormal effects of UV and VL on skin
- PHOTOSENSITIVITY: Abnormal response to “ordinary “ light exposure
- PHOTOMEDICINE: Study of skin diseases caused by radiation in UV and visible spectra

Terrestrial radiation

- It is the infrared radiation emitted from the atmosphere

1. Ultraviolet- 100 to 400nm
2. Visible - 400 to 700 mm
3. Infrared- > 700nm


10^{-12}
10^{-9}
1nn
10^{-6}
1000 nm
10^{-3}
1mm
10^{0}
1m
10^{3}
1km
Cosmic rays
X-rays
Ultraviolet (UV)
Infrared (IR)
Microwaves
Radar
Radio
Broadcast band
Short Wavelengths
Long Wavelengths
Ultraviolet (UV)
Infrared (IR)
400 nm
500 nm
600 nm
700 nm
© Buzzle.com

Meet ultraviolet

- Radiation with wavelength shorter than light but longer than X ray
- It has both benign and malignant impact on the health of a living being

- **UVA: 400 to 315nm**
  - relatively long wavelength
  - represents close to 95% of the UV Rays
  - skin aging, wrinkles
  - damages keratinocytes in basal layer of epidermis = skin cancers
  - dominant tanning ray

Meet ultraviolet

- **UVB: 315-250 nm**
  - Medium wavelength
  - Only part passes through the atmosphere
  - Damages skin cells directly
  - Main ray that causes sunburn

- **UVC: 280-100nm**
  - Most harmful
  - Does not reach the earth surface
  - Completely filtered by ozone layer

Fitzpatrick skin types

I
White
Always burns, never tans.

SPF **30+** everyday

You tend to have very pale, porcelain or ivory toned skin, like The Help actress **Emma Stone**. You always burn in the sun, and your skin could have a naturally reddish undertone. Your eyes are most likely blue, gray or green and you might rock a head of gorgeous blonde or red hair.

Plus: Anne Hathaway, Cate Blanchette, Prince Harry, Liam

II
Beige
Usually burns, tans with difficulty

SPF **30+** everyday

With **Type II** skin, you have a fair or cream-colored complexion, often coupled with subtle beige undertones like actress **Lucy Liu**. Your eye and hair colour could fall anywhere along the range of light to dark, and you might have a handful of cute freckles as well. Although you tend to burn in the sun, you are able to tan occasionally.

Plus: Drew Barrymore, Jennifer Aniston, Brad Pitt, Zac Efron

III
Light Brown
Sometimes burns, slow tanning

SPF **30+** everyday

Like top actress **Sandra Bullock**, people with **Type III** skin are often described as having a golden, honey-hued skin tone. Women and men with light olive coloring also fit into this skin type. At the beginning of summer, you may find that you burn easily, but you can gradually build a sun-kissed glow by the end of the season.

Plus: Demi Moore, Lisa Ling, John Stamos, Matthew McConaughey

IV
Medium Brown
Rarely burns, fast tanning

SPF **15+** everyday

Just like Slumdog Millionaire star **Freida Pinto**, your skin is a gorgeous caramel tone, and tans quickly without burning. With **Type IV** skin, you most likely share her dark hair and probably have dark eyes that range from hazel to ebony as well.

Plus: Eva Mendez, Jessica Alba, Taylor Lautner, Dev Patel

V
Dark Brown
Rarely burns, fast & easy tanning

SPF **15+** outside

If you have **Type V** skin, your skin tone matches that of award-winning singer songwriter **Beyoncé**, and might range from radiant bronze to a rich brown. Like **Beyoncé**, both your eyes and hair are dark. You experience sunburns very rarely, and generally tan quickly and easily.

Plus: Mindy Kaling, Tyra Banks, Barack Obama, Craig David

V
Black

SPF **15+**

Like supermodel **Naomi Campbell**, who has graced over 400 magazine covers, your skin tone falls in the range of deep mahogany to espresso. You almost never have sunburns, and tan quickly and deeply during the summer. With **Type VI** skin, you have both dark hair and dark eyes.

Clinical effects of UV radiation

- **Acute**
  - Erythema
  - Tanning
  - Immunomodulation
- **Chronic**
  - Skin cancer
  - Photoaging

Erythema

- UV radiation induced inflammation
- Sunburn - common, visible, acute inflammatory response to excessive exposure to UV radiation
- Associated with redness
- Wavelength around 300nm is most erythmogenic
- 307.5 causes max burning

Tanning

- **Immediate pigment darkening**
  - Due to immediate photo-oxidation of existing colourless melanin precursors to UVA and visible radiation
  - Fades within 15 minutes
  - Almost undetectable in fair skinned individuals
  - Easily observed in skin type 4 or darker
- **Persistent pigment darkening**
  - response to higher UV dose >10 J\cm²
  - Peaks 2 hours post radiation
  - Lasts for 1-5 days
  - Due to persistent oxidation of melanin precursors
  - End point used to assess UVA protection of sunscreens

Tanning

- **Melanogenesis or delayed tanning**
  - Facultative pigmentation or neomelanogenesis
  - Stimulation of new melanin synthesis by basal epidermal melanocytes
  - Transported via dendrites to adjacent keratinocytes
  - Redistributed towards skin surface

Immunomodulation

- **Effect on antigen presenting cells:**
  - depletes the epidermis of Langerhans cells
- **Effect on T cells:**
  - Stimulates the circulating suppressor T cells - alters the ability of lymphocytes to respond to mitogens and antigens
  - Suppression of delayed hypersensitivity and contact hypersensitivity- reduction of tumour rejection – increased incidence of malignancies.
  - Alters the proportion of circulating T cell sub types.
  - Release of inflammatory mediaters-IL-1 and IL-6 which are immunosuppressive and alter cell trafficking.
  - Other effects-impairment of immunological responses of the epidermal keratinocytes and lymphocytes

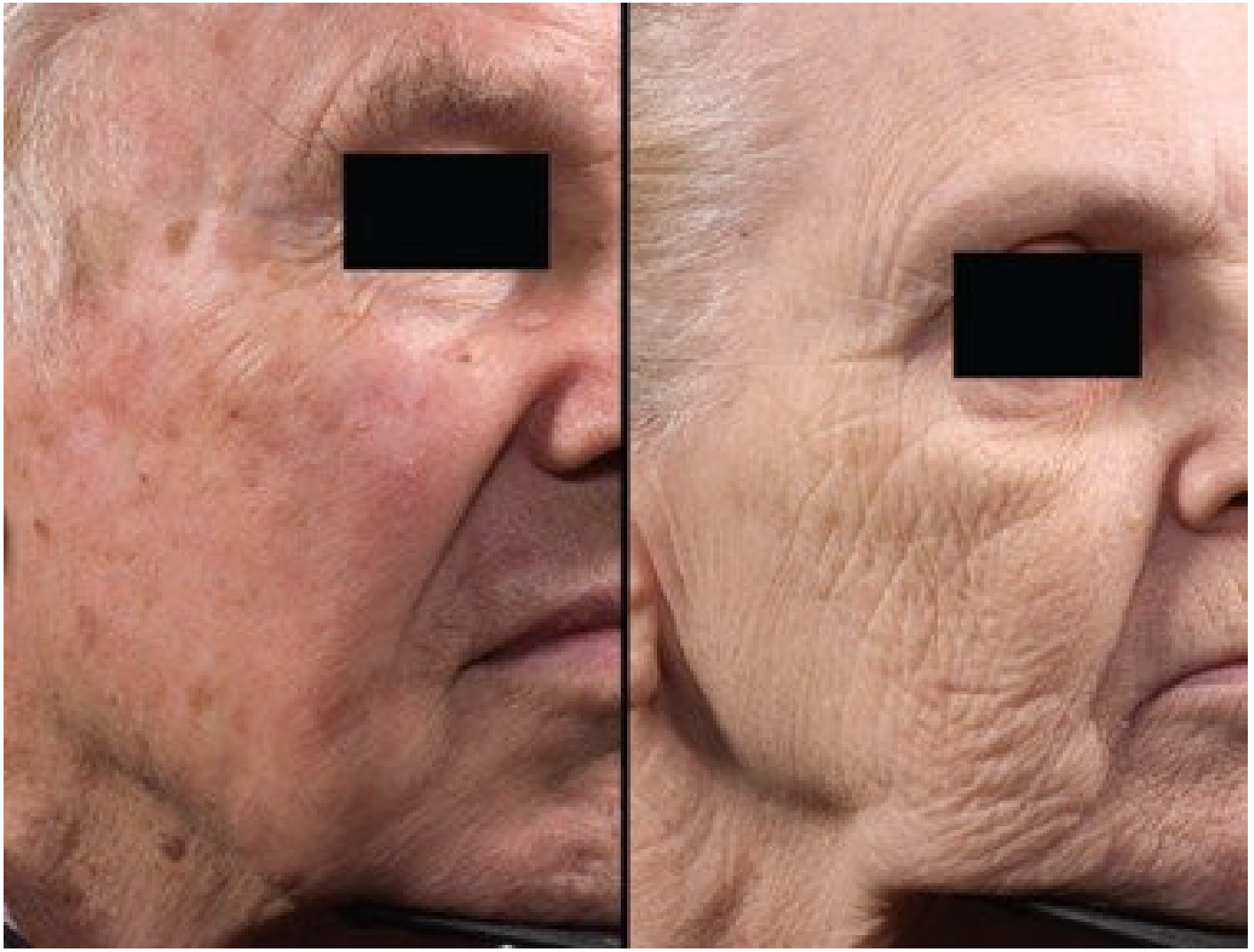
Skin cancer

- Malignant melanoma
- Non melanoma skin cancers

Photoaging

- Process of skin aging which has been accelerated by chronic solar exposure.
- Also known as DERMATOHELIOSIS.
- Clinically distinct from chronological aging

Photoaging



Phototherapy

- Form of treatment of a skin condition involving the administration of non ionizing radiation in a controlled manner to skin.

- 1400 BC: India- vitiligo patients were given certain plant extracts and exposed to sun.
- 1903: Neils Finsen received Nobel prize for therapeutic results with UV radiation in Lupus vulgaris
- 1974: Parish et al reported useful role of high intensity UVA tubes in combination with psoralens for psoriasis.
- 1978: Wiskemann introduced irradiation cabins with broad band UVB tubes for treatment of psoriasis and uremic pruritus.
- 1988: NBUVB phototherapy was introduced by van Weelden et al and Green et al.

Therapeutic modalities

- UVB
- LONG WAVE UVA
- PUVA (BALNEOTHERAPY)
- EXTRACORPOREAL PHOTOPHERESIS
- PHOYODYNAMIC THERAPY
- TARGETED PHOTOTHERAPY

UVB

- UVB- 280-320 nm
- Full spectrum(BBUVB)- 270-350nm
- Narrow band(NBUVB)- 311-313nm
- NBUVB is now the gold standard
- Advantage - decrease in the erythmogenic wavelength with a 5 fold increase in longer wavelengths resulting in increased therapeutic effect
- Mechanism of action in Psoriasis- anti-inflammatory, immunosuppressive and cytotoxic.

UVB

- **Minimal erythema dose (MED):** the dose of radiation that produces minimal, just perceptible erythema at 24hrs post radiation
- **Starting dose:** 70% or 50% of MED
- **Increments:** As the skin acclimatizes to UV, by epidermal thickening and pigmentation, it is necessary to increase the dose
  - low increment- 20%
  - high increment- 40%
- **Frequency:** 2 or 3 times per week

UVA-1

- Long wavelength – 320 - 400 nm while filtering the erythmogenic UVA and UVB wavelengths
- Penetrates deeper in the dermis
- Induces interstitial collagenase and cytokines
- Softening of sclerotic skin

- Doses
  - High: >60 J\cm²
  - Medium: 30-60 J\cm²
  - Low: 10-20 J\cm²

PUVA

- Psoralen + UVA
- Inhibits DNA replication
- Langerhans cell depletion
- Immunosuppressive effect on T lymphocyte functions
- Migration and restoration of Th17/regulatory T cells imbalance in Psoriasis

PUVA

- The drug psoralen has no therapeutic effect of its own. Only produces effect when patient is exposed to UV radiation
- Drugs used:
  - Methoxsalen (8-methoxypsoralen)
  - Bergapten (5-methoxypsoralen)

PUVA

FDA APPROVED INDICATIONS

Psoriasis

Vitiligo

OTHER DERMATOLOGIC USES

Neoplastic

Chronic hand dermatitis

Palmoplantar pustulosis

Lichen planus

Parapsoriasis

Pityriasis lichenoides

Seborrheic dermatitis

Atopic dermatitis

Papulosquamous/dermatitis

Histiocytosis X

Mycosis fungoides/Sézary sy.

Lymphomatoid papulosis

Balneotherapy

- Process of delivery of 8 methoxy psoralen or different salt solutions through bath with a subsequent UVA or UVB irradiation
- Delivery of psoralens by bath prevents systemic side effects associated with oral PUVA
- Advantage of shorter and selective photosensitization leading to significantly lower cumulative UVA exposure
  - Bath PUVA
  - Bathing suit PUVA
  - Soak PUVA
  - Turban PUVA

Extracorporeal photophoresis

- A discontinuous leukapheresis procedure that combines the administration of 8-MOP with extracorporeal UVA irradiation to a fraction of peripheral blood leukocytes
- It targets the effects of photochemotherapy directly to circulating pathogenic leukocytes
- Photo testing not necessary as irradiation occurs outside the body in a machine.
- Frequency: 2-3 successive days once a month
- During 1 treatment session 5%-10% of the circulating T cell pool is treated
- Duration about 6 months

PUVA

- **Minimal phototoxic dose (MPD):** measured 2 hours (or 2.5 hours for 5 MOP) after patient has ingested standard dose of psoralen. Test site read after 72-96 hours
- **Starting dose:** 40% of MPD for topical PUVA
- 70% of MPD for oral PUVA
- Increments: 20% to 40%
- Frequency: twice daily as erythema is delayed
- **Eye protection: following ingestion of psoralen, patients are required to wear UVA absorbing glasses before therapy and for at least 12 hours post therapy(children 24 hours)**

Puva contraindications

- Dysplastic nevus syndrome
- SLE
- Dermatomyositis
- Xeroderma pigmentosum
- Bloom syndrome
- Unreliable patients
- Medically unfit

Photodynamic therapy (PDT)

- Photodynamic reaction, also known as the photodynamic phenomenon has been known since the end of the 19th century
- At the beginning of the 20th century, **Tappeiner and Jesionek** published a report on his experiments with the treatment of spinalioma, basal cell carcinoma and lupus vulgaris by topically applied eosin and subsequent irradiation
- Tappeiner was also the first to treat the reactions with a photoactive substance, followed by irradiation in the presence of oxygen, the term "photodynamic effect" however, the results of his work were forgotten
- Since the 1980s, there has been a resurgence of interest in this treatment method

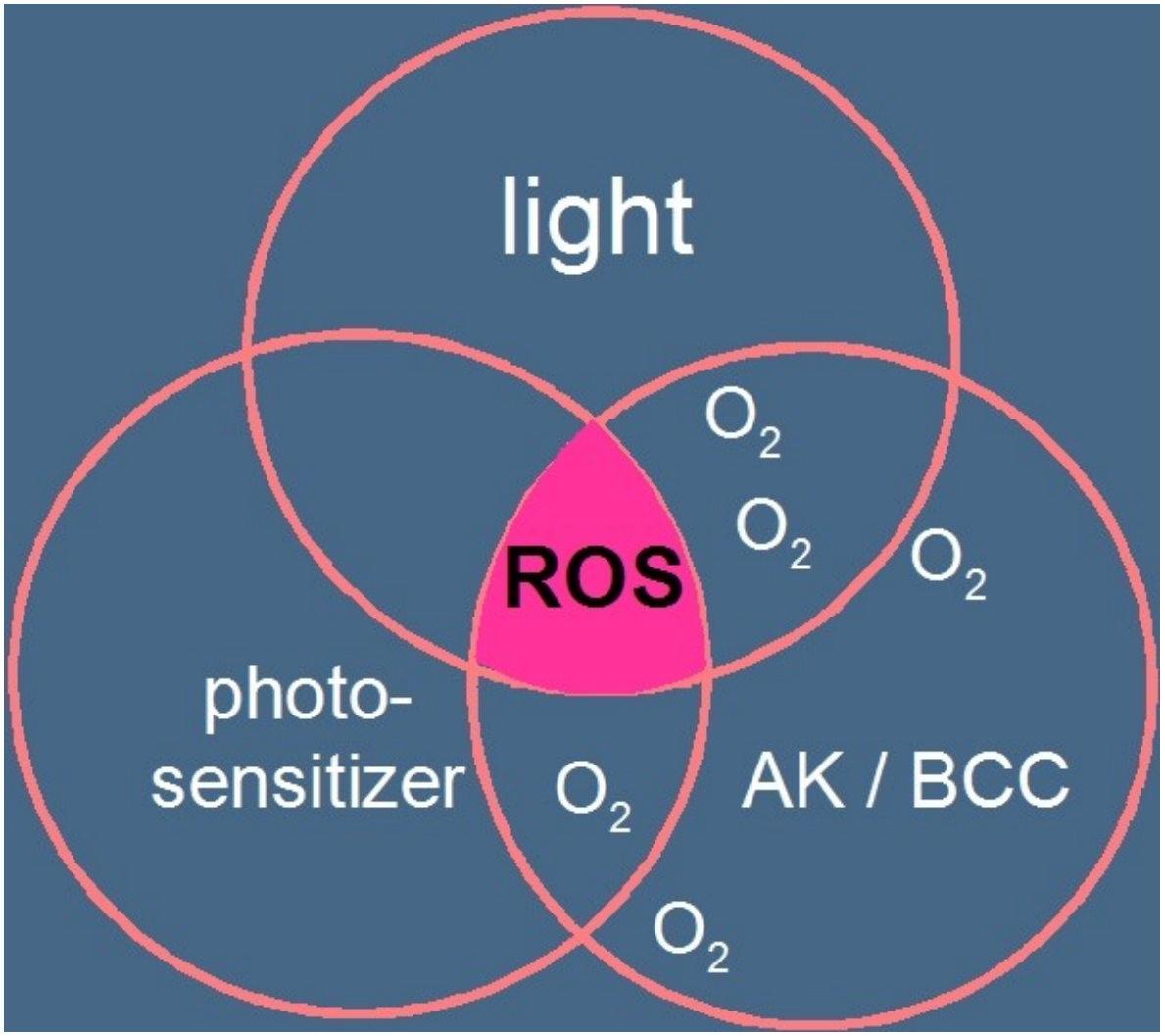
Photodynamic therapy (PDT)

- In recent years, in addition to dermatology, PDT has also been used in other medical fields, such as ENT, gastroenterology, pneumology, gynecology and urology

Photodynamic therapy (PDT)

- Is a modern, non-invasive, therapeutic and diagnostic method used in the treatment of mainly skin tumors
- Consists in the local application of a photosensitizer to the treated lesion (especially a tumor) followed by irradiation with visible light
- PDT principle - based on the photodynamic effect
- **Photodynamic effect:** photosensitizer molecules activated by visible light excite oxygen to a reactive state, with the formation of free oxygen radicals "ROS" (reactive oxygen species), which then damage both tumor cells and endothelium of blood vessels that supply the tumor with oxygen and nutrients

PDT - mechanism of action



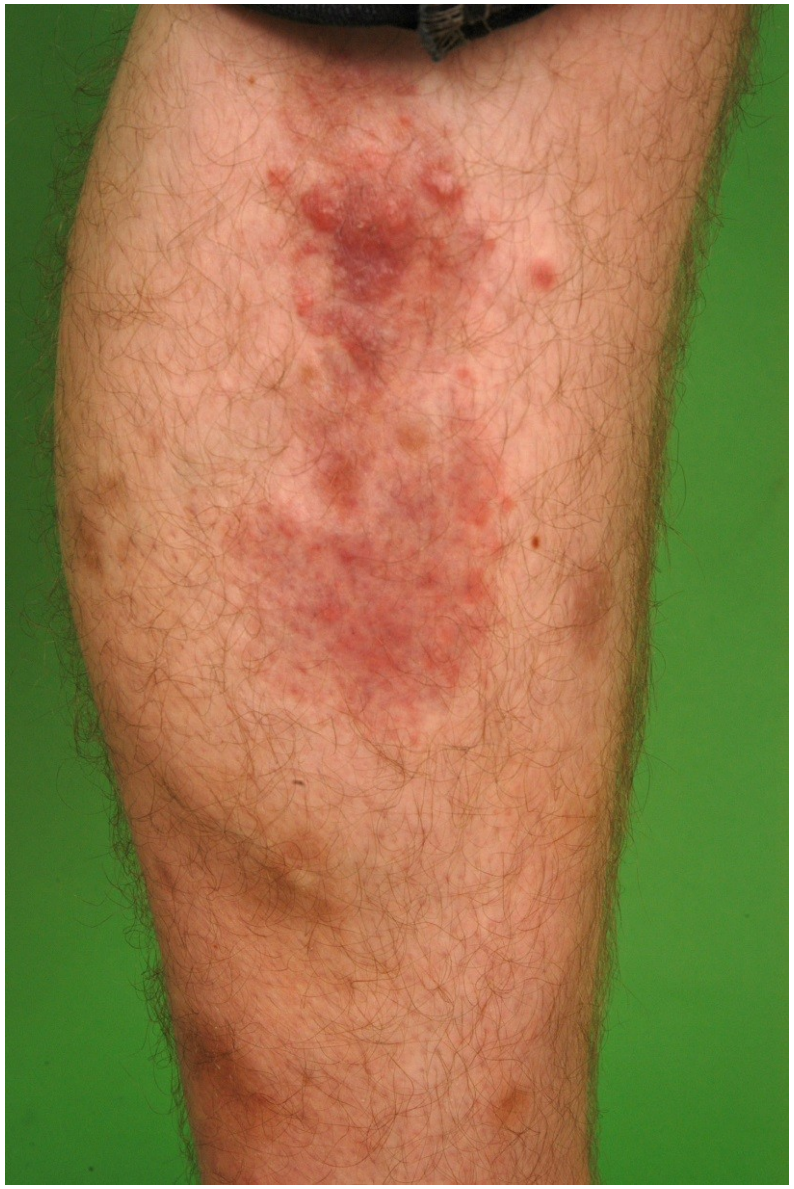
Statistics od PDT

Treatment success rate - 91%

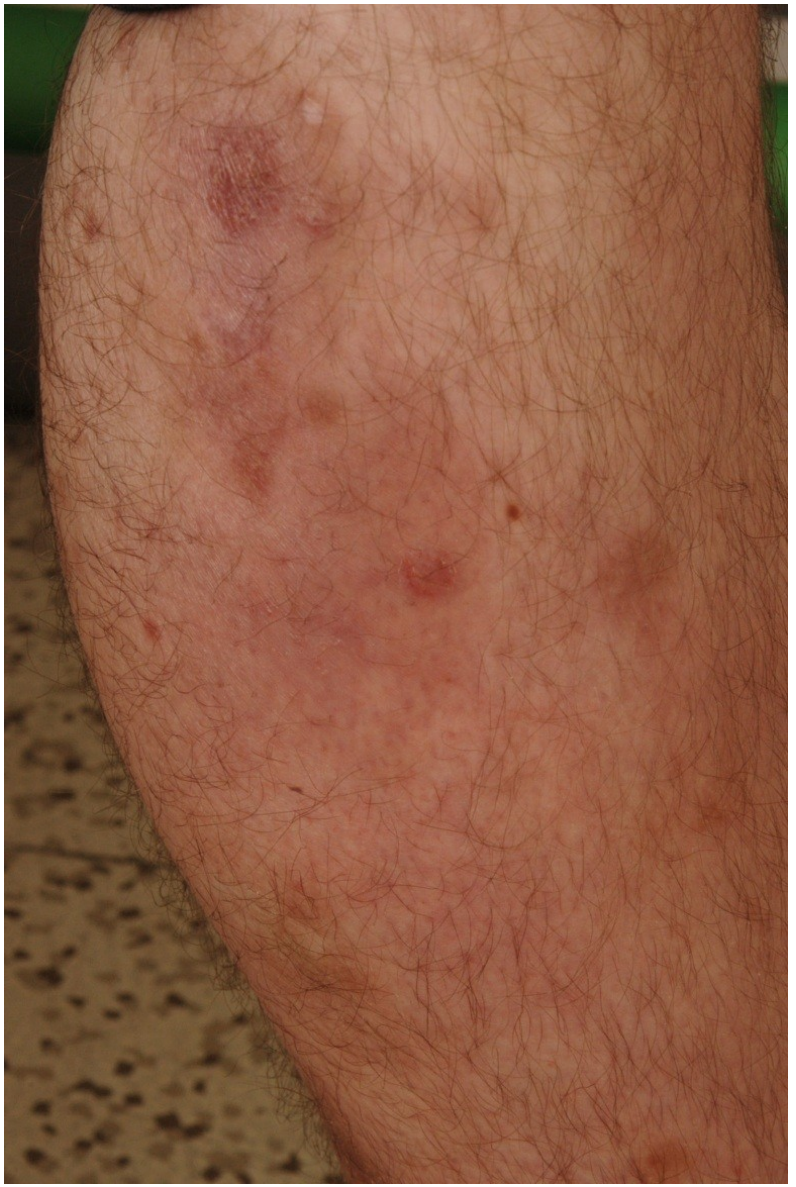
(the remaining 9% are patients who relapsed within 6 months of the last PDT course and patients who did not respond to the therapy)

PDT

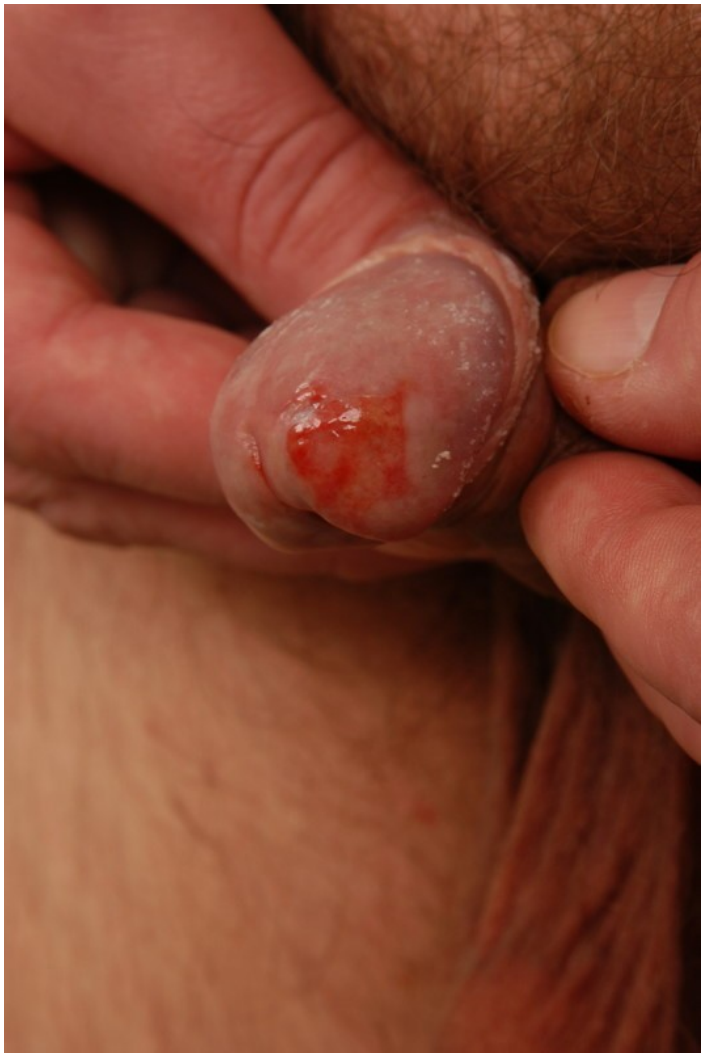
Before PDT



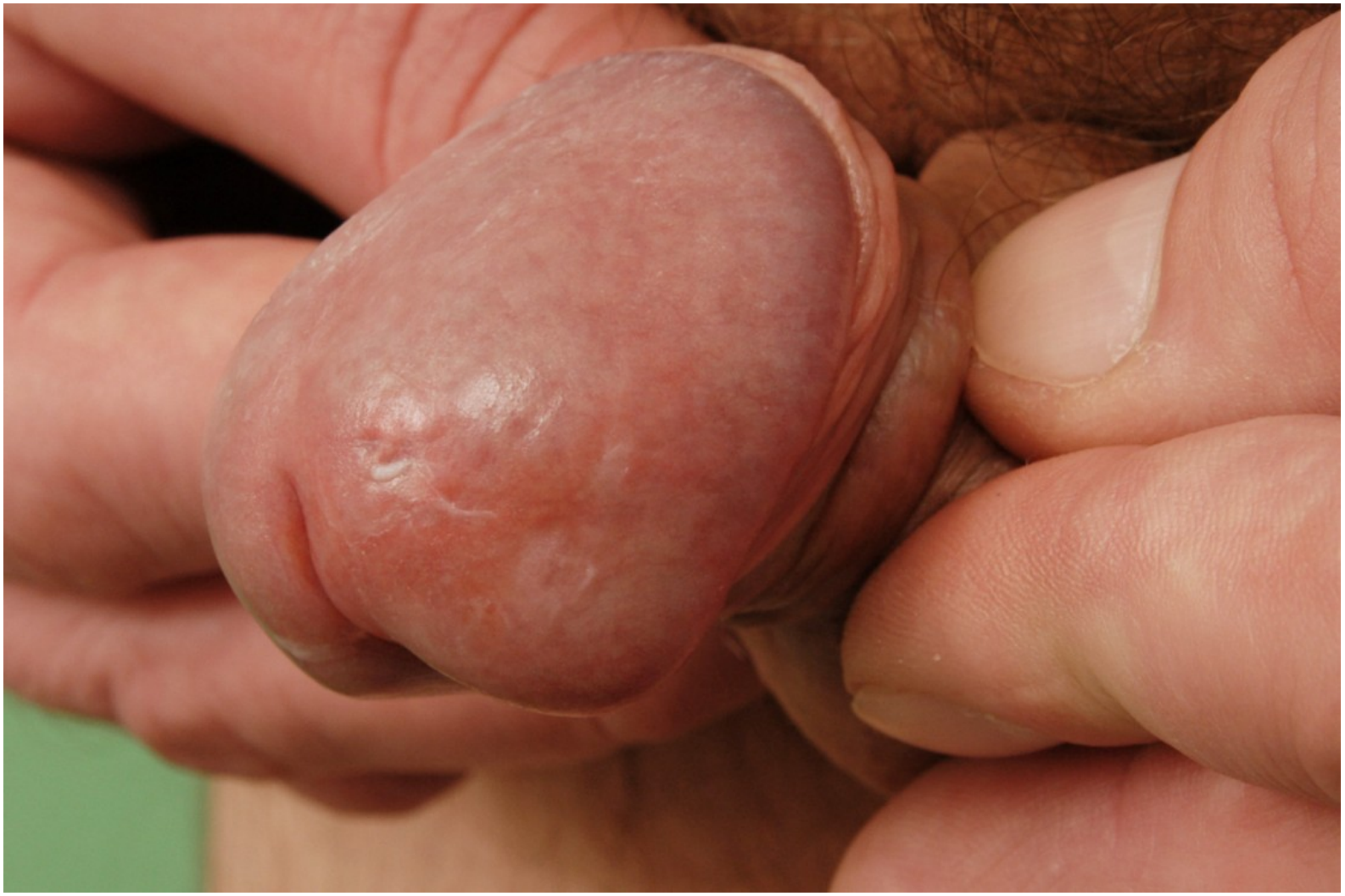
After III. courses of PDT



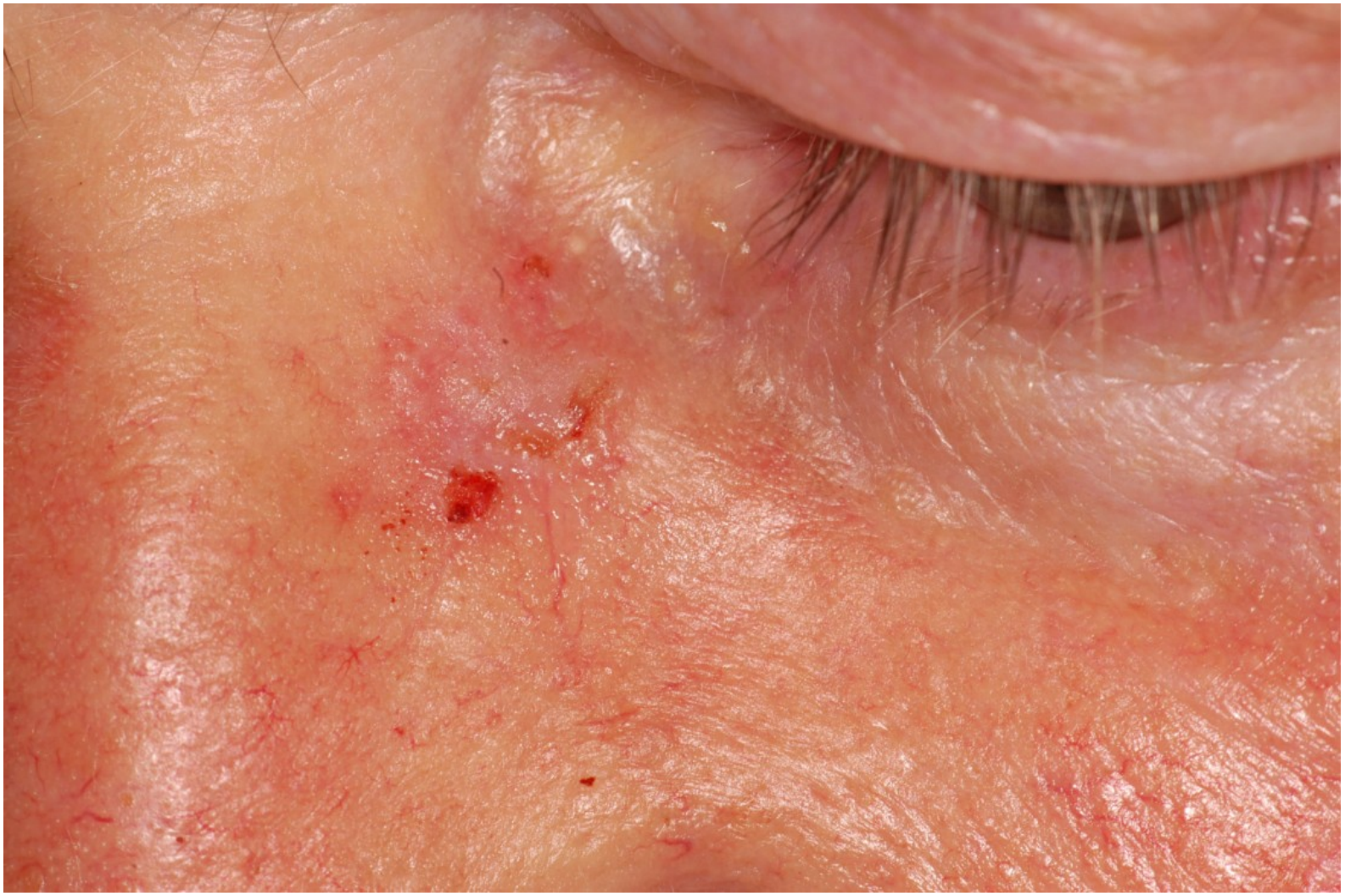
Before PDT



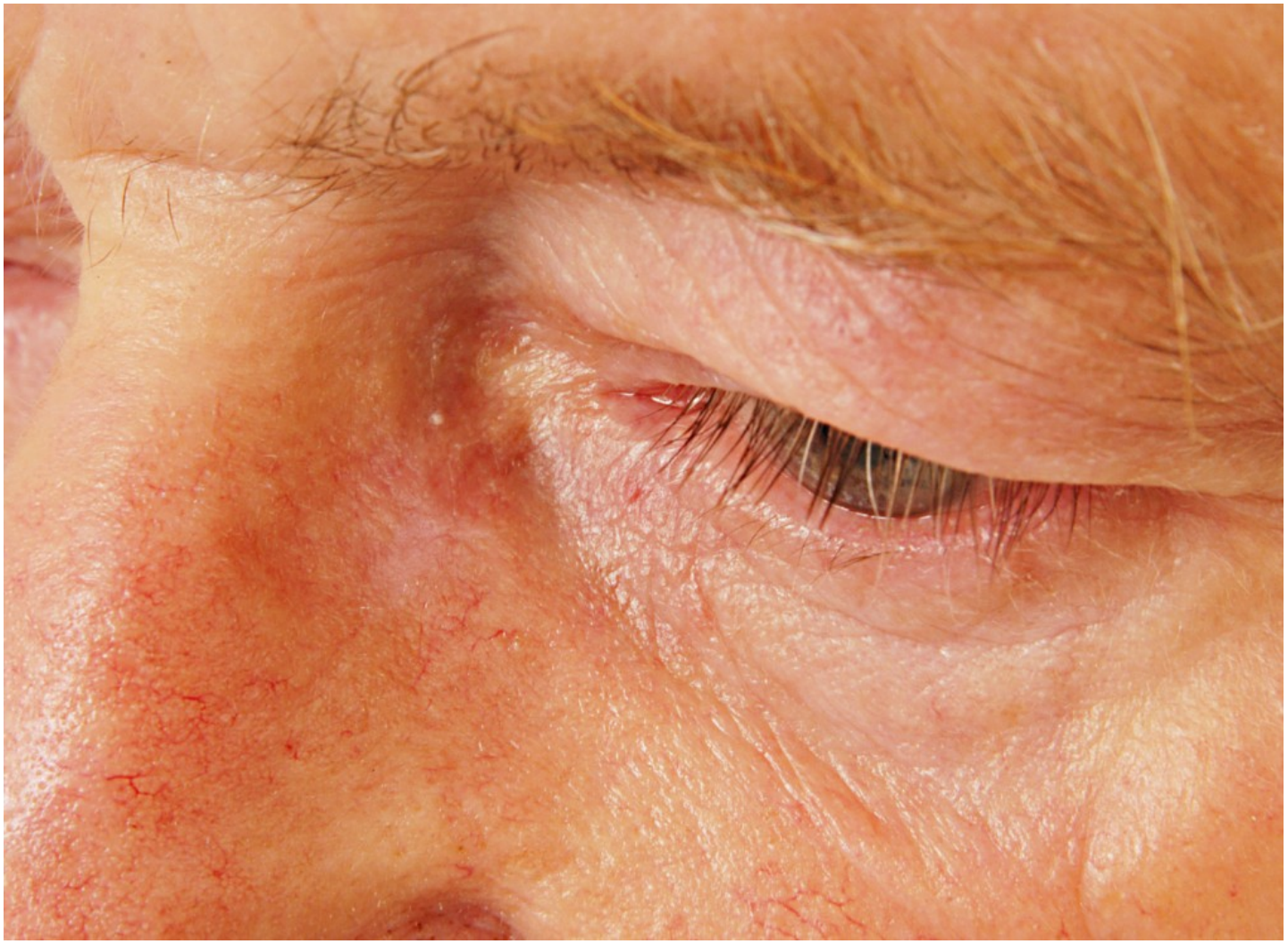
After IV. courses of PDT



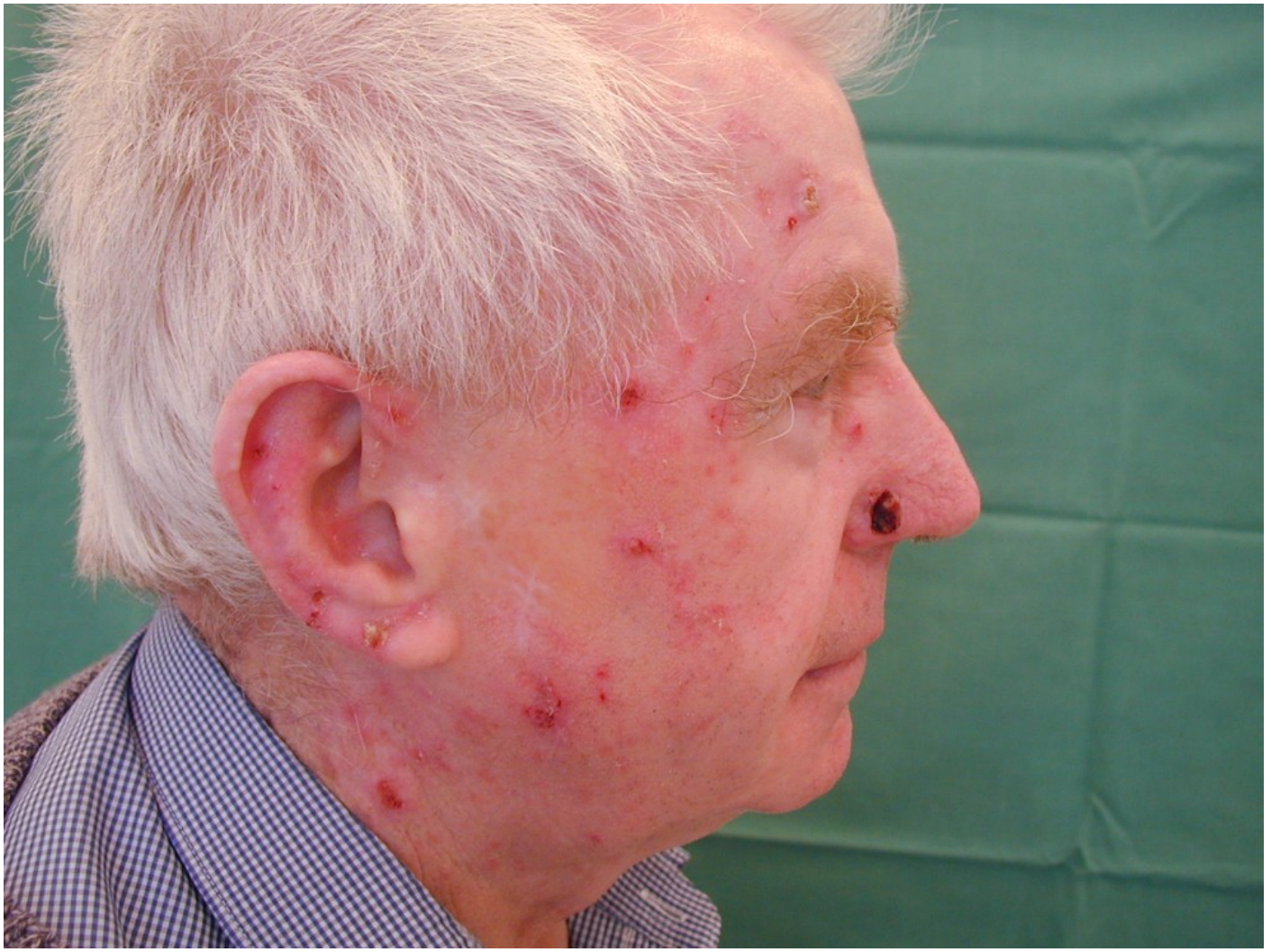
Before PDT



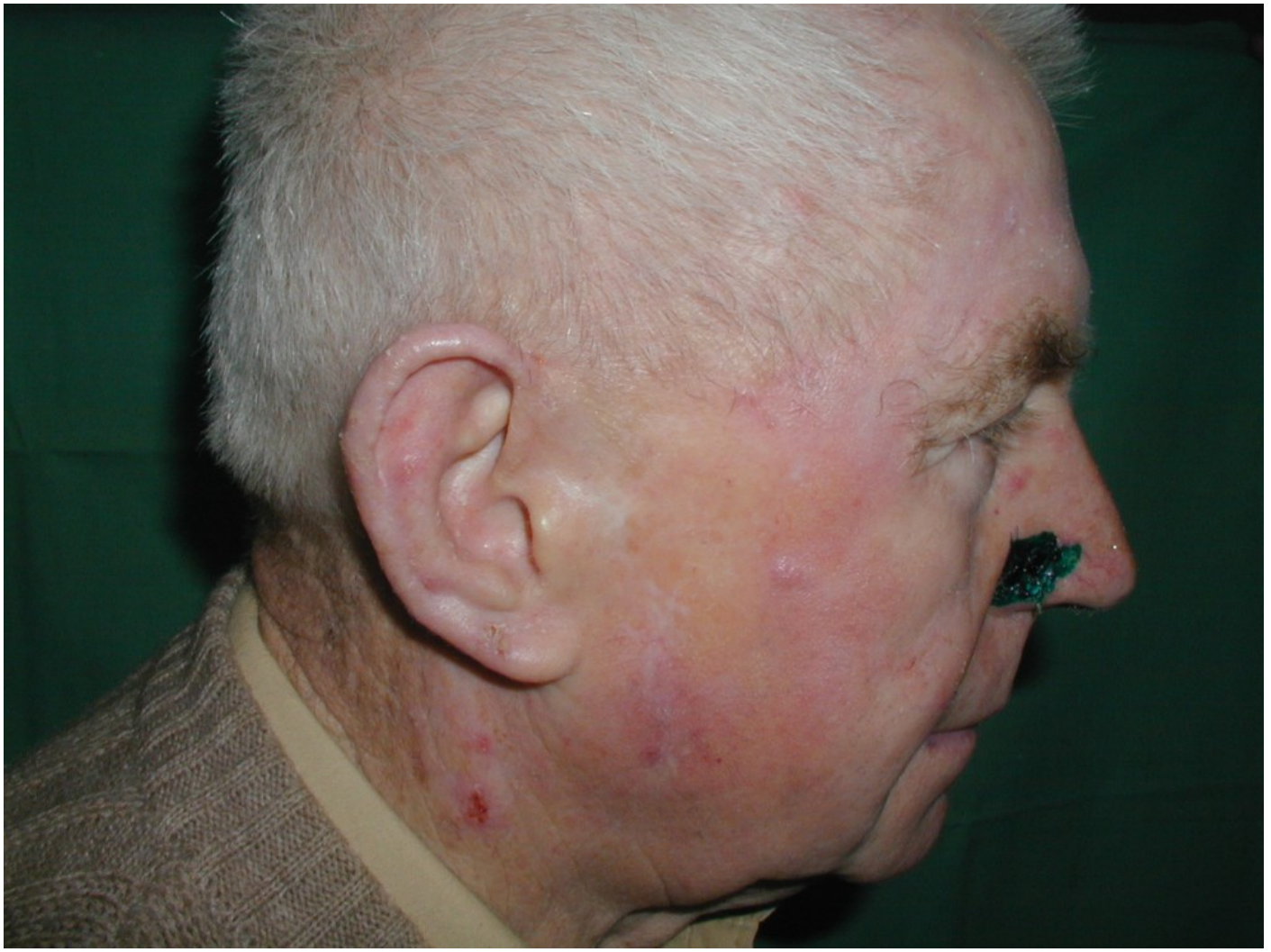
After II. courses of PDT



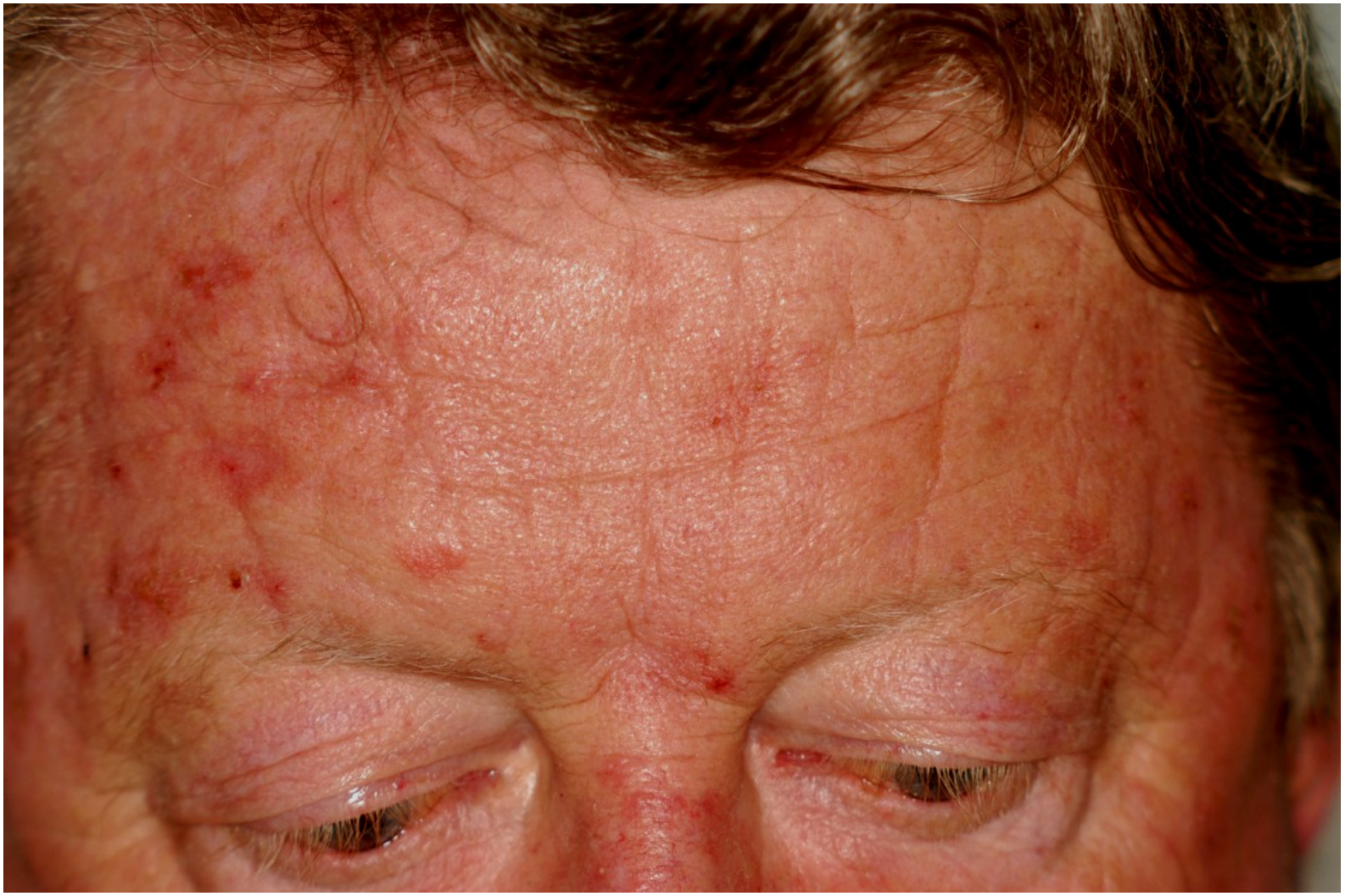
Before PDT



After II. courses of PDT



Before PDT



After IV. courses of PDT