Melasma is a long-lasting disorder

- Spontaneous improvement during winter
- High rate of recurrences (after summer+++)
- Impact of UVB and UVA well demonstrated (check for PPD index)

Role of the visible light

- Visible light induces significant and long lasting hyperpigmentation in dark skin types (skin types III and higher)
- Only the shorter wavelengths of the visible light are propigmenting
- Mechanisms involved appear to be different to those involved in UVB-induced pigmentation

Impact of protection against shorter wavelengths of visible light in melasma relapses

- Monocentric randomized comparative study on 40 patients with melasma
- Begin of the study the two first weeks of April
- End of the study the two first weeks of September
- Evaluation on MASI performed on standardized pictures (VISIA, Canfield) by two independent physicians blinded to the sunscreen used

Development of a visible light protection index

- Interest of combining protection against UVB, UVA and shorter wavelengths of visible light for optimal protection in melasma

Conflicts of interest

- Research grants and/or honoraria:
  - Bioderma
  - Beiersdorf
  - DELEO
  - Galderma
  - L’OREAL
  - ISIS Pharma
  - SVR
  - Synrise
  - Syneron-Candela
Laser and light-based treatments of melasma

- Q-switched ruby, alexandrite or Nd:YAG lasers:
  - Mild to moderate efficacy
  - Constant relapses and high rate of PIH

- Intense pulsed light:
  - Mild to marked improvement reported in several studies
  - Combination with Trio > Trio alone
  - Decrease in MASI score remains at 44.9% at 12 months in combination group Vs none in Trio alone
  - Risk of PIH mostly in skin type IV to VI

Low-fluence QS laser and melasma

- Low-fluence QS 1064nm laser showed promising results in pilot studies
- Prospective randomized split face study
  - 22 patients with melasma
  - 2% HQ vs 2%HQ + low-fluence QS ND:YAG 1064nm
  - HQ started 2 weeks before the laser treatment
  - 5 weekly sessions of laser in total (spot 6 mm; fluence 3 to 3.8 J/cm²)
- Evaluation:
  - MASI + colorimeter
  - Follow-up: 12 weeks after the end of the treatment

Results:
- End of Tx: ++
- At 12 weeks: Relapse in all the patients + 4 PIH

Non ablative fractional laser for melasma

- 1550nm fractional laser showed interesting results for treating melasma in preliminary studies
- Open study:
  - 25 patients
  - One session every month for 4 months
  - Evaluation: MASI and spectrophotometry
  - Follow-up: 6 months

Low-fluence QS laser side effects

- 14 cases of hypochromia sequella following repetitive use of low-fluence QS laser (9 for photo ageing and 5 for melasma)

  - No or weak interest of low-fluence QS laser for treating melasma
Results:

- After Tx:
  - Marked improvement in 24% of patients
  - At 6 months:
    - Constant but slight relapses
    - MASI: mean 7.6 (3.2–14.7) at M0 to 6.2 (1.8–10.2) (p=0.03)
    - Worsening of the hyperpigmentation in 13% of cases

Non ablative fractional laser for melasma

- Prospective comparative randomized study
- 20 melasma patients, skin types II to V
- Non ablative 1550nm fractional erbium laser
  - 8 passages (MTZ 2000 to 2500/cm²; 10mJ)
  - 1 session every 2 weeks for 8 weeks
- Vs Kligman’s trio
  - 1/d for 8 weeks
  - Evaluation blinded to the treatment received
  - Main criterion: PGA
  - Follow-up 3 wks, 3 and 6 months after the end of the treatment

Laser thulium 1927 nm for melasma

- Encouraging results in a pilot study in 2012
- Retrospective study in 20 women with long term follow-up
  - Skin type II to IV
  - 10–20 mJ/cm² with 60–70% coverage
  - Evaluation on MASI score up to 12 months
  - 15 patients seen at 12 months
  - Recurrence in 7 out of 15 patients
  - 2 PIH

Picosecond laser for melasma

- Prospective, randomized, split-face, controlled study
- 40 patients with melasma
- 7 week 2% HQ (daily) on one side of the face
- 7 week 2% HQ (daily) + 5 weeks 532/1064nm picosecond laser (weekly)
- Follow-up 18 weeks
- Main criteria:
  - mMASI on standardized pictures
  - 38 patients in per protocol analysis and 39 in mITT

Revisiting melasma pathology

- Increased number of melanocytes, increased epidermal and dermal melanin
- 93% moderate/severe elastosis
- 84% increased melanocytes
- Increased melanin at all level of the epidermis
- Dermal melanin in 36% with increased dermal melanin and melanophages (12%)
- 70% mild/moderate elastosis
- No increase in melanocytes
- Melanin not increases in the epidermis
- Dermal melanin noted in 36% of perilesional cases in Korean skin
Melasma, a vascular disorder?

![Image](image1.png)

**Melasma Transcriptomic study**

- **Identification of genes differentially expressed in melasma lesional skin**
  - 12 patients (only 10 evaluated)
  - 279 genes significantly up or down-regulated in melasma lesional skin
  - Up-regulation of many melanin bio-synthesis-related genes as well as melanocytes markers
  - Increased expression of a subset of Wnt pathway modulator genes
  - Prostaglandin metabolic process up-regulated
  - Genes that regulate fatty and metabolism differentially expressed

- **Hierarchical clustering of lesional and perilesional normal skin of 10 melasma patients.**
  - A hierarchical clustering based on the genes that were considered as differentially expressed, where red/green color is the higher expression/lower expression groups, respectively.

**Melasma, a vascular disorder?**

- **Vessel size (µm²)**
- **Vessel density (mm²)**
- **Vessel area (%)**

<table>
<thead>
<tr>
<th>Perilesional normal skin</th>
<th>Lesional skin</th>
<th>Perilesional normal skin</th>
<th>Lesional skin</th>
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<tbody>
<tr>
<td>Vessel size</td>
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<tr>
<td>Normal</td>
<td>Lesion</td>
<td>Normal</td>
<td>Lesion</td>
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</tbody>
</table>

**Regulation of skin pigmentation: A complex process**

- **UV**
- **Keratinocyte**
- **Fibroblasts**

- Crucial role of endothelin 1 secreted by endothelial cells

**Role of skin microvascularization in pigmentation**

- 100 benign vascular lesions
- High magnification digital dermoscopy (×50 – ×200)
- Laser confocal microscopy and histology

- Significantly increased pigmentation above and around vascular lesions
Mechanism of action of tranexamic acid in melasma?
- Prospective study with biopsies after 12 weeks of treatment with TA
- TA might act on melasma through a decreased production of endothelin 1

PDL treatment for melasma
- Prospective randomized controlled slip face study
- 18 patients with melasma (skin types II to IV)
  - Intervention:
    - Stabilized triple combination cream
      - Applied once a day for 4 months on the entire face
    - PDL
      - Start after 1 month of triple combination cream
      - 3 sessions (every 3 weeks) on 1 hemi face
        - 1st passage with pressure hand piece 10mm, 1.5ms, 7J/cm²
        - 2nd passage with hand piece 7mm, 20ms, 10J/cm², DCD 30/40
  - Blinded evaluation after 1 summer

Results
- Mean difference between the 2 groups in 'hemiMASI' score at V4 was 1.9 points (p=0.019)

PDL and melasma
- Promising results
- Need confirmation in larger series
- Optimal parameters and schedule of treatment have to be determined
  - Results confirmed in a recent Korean prospective trial (IPCC 2014 Pr YH Kang) and in a recent case report with long term follow-up
  - Risk of PH in skin types IV and higher that limits this approach
- Interested of targeting vessels for treating melasma
Melasma =
UVB + UVA + Blue light + pigmentation + vascularization + sloughing and fibroblast secreted factors + altered basal membrane

Global therapeutic approach

- Photon protection (including against shorter wavelengths of visible light)
- Discuss discontinuation of hormonal treatment +/- Avoid friction

SUN Melasma Photoprotection+++

Discuss discontinuation of hormonal treatment +/- Avoid friction

Melanoma Photoprotection+++

Risk of PIH in skin types IV and higher

Maintenance treatment:
- Photoprotection+
- Cosmetic blanching cream
- Risk of PIH in skin types IV and higher
- Of label used
- To be measured

Peeling: risk of PIH
- 1550 nm fractional laser (risk of PIH)
- 1924 nm thulium fractional laser (few data and risk of PIH)

Chemical approaches to prevent visible light-induced pigmentation

Success
- HQ 5%
- Tretinoin 0.1%
- Dexamethasone acetate 0.1%

Failure
- To be determined

Off-label used