Excimer laser treatment for vitiligo

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Conflict of Interests Disclosure

I was an author in a RCT of excimer laser combined with topical steroids
• Some definitions

• The concept of targeted repigmentation

• Excimer laser treatment of vitiligo: the evidence

• Future perspectives
Definition of a “laser”

• The term "laser" originated as an acronym for Light Amplification by Stimulated Emission of Radiation

• A laser is a device that emits light through a process of optical amplification based on the stimulated emission of electromagnetic radiation
Characteristics of a laser light

• **Monochromatic**: it consists of one single color or wavelength. The light is extremely pure and consists of a very narrow spectral range.

• **Directional**: the beam is well collimated (very parallel) and travels over long distances with very little spread.

• **Coherent**: means that all the individual waves of light are moving precisely together through time and space, i.e. they are in phase.
Excimer laser vs lamp

- An excimer laser typically uses a combination of a noble gas (argon, krypton, or xenon) and a reactive gas (fluorine or chlorine).
- Under the appropriate conditions of electrical stimulation and high pressure, a pseudo-molecule called an excimer (or in the case of noble gas halides, exciplex) is created, which can only exist in an energized state and can give rise to laser light in the ultraviolet range.
- Emission of excimer molecules is also used as a source of spontaneous ultraviolet light (excimer lamp).
Xenon, pulsed light laser
308 nm monochromatic light

Spot 2x2cm

Pulse energy 2-3 mj/cm²
Duration of pulse 30 nsec
• Some definitions
• The concept of targeted repigmentation
• Excimer laser treatment of vitiligo: the evidence
• Future perspectives
Repigmentation

• Vitiligo repigmentation depends on a viable melanocyte reservoir
• In many patients with vitiligo repigmentation is possible when pigment cells are stimulated with appropriate treatment
• Melanocytes for repigmentation by medical methods arise from three main sources: (a) the hair follicle unit; (b) unaffected melanocytes within areas of depigmented epidermis, and (c) melanocytes located at the edge of vitiligo lesions
Vitiligo

Generalized
Depigmented patches on the hands, neck, genitalia, limbs, and face

Segmental
Unilateral distribution (Blascko lines)

Focal vitiligo
Stigma
(After E. Goffman, 1963)

A physical mark that would be placed on a person to signify them as deviant, such as branding of slaves.

Today stigma refers to the social marks that are defined as undesirable and deviant. They range from physical disability to perceived weaknesses.

Intrinsic in the discussion of stigma is the issue of deviance.
“Veste quae ex duobus texta est, non indueris” (Leviticus, 19,19)

“Clothes which are made of two different materials are not allowed”
Spotted surfaces or animal coats, has been associated since Medioeval age, in Western countries, with the idea of impurity or disease (M. Pastoreau, 1991)

(Dante, Divina Commedia, canto 1)

Ed ecco quasi al cominciare dell’erta una lonza leggiera e presta molto che di pel maculato era coperta...
Xenon, pulsed light laser
Targeting vitiligo areas
Avoiding tanning nonaffected areas
ORS melanocyte transferral

Extraction of outer-rooth sheet (ORS) melanocytes

Suspension in isotonic saline solution

Pre-treatment of target site by microneedling

Transferral of ORS melanocyte suspension to target site
Repigmentation by Outer-Root-Sheath-Derived Melanocytes: Proof of Concept in Vitiligo and Leucoderma

Wolfgang Vanscheidt\textsuperscript{a} Thomas Hunziker\textsuperscript{b}

\textsuperscript{a}Dermatologische Gemeinschaftspraxis, Freiburg, Germany; \textsuperscript{b}Department of Dermatology, University of Bern, Bern, Switzerland
Guideline for the diagnosis and management of vitiligo

D.J. Gawkrodger, A.D. Ormerod, L. Shaw, I. Mauri-Sole, M.E. Whitton,*† M.J. Watts, A.V. Anstey, J. Ingham‡ and K. Young‡

British Association of Dermatologists, 4 Fitzroy Square, London W1T 5HQ, U.K.
*Vitiligo Society, 125 Kennington Road, London SE11 6SF, U.K.
†Cochrane Skin Group, Centre of Evidence Based Dermatology, King’s Meadow Campus, University of Nottingham NG7 2NR, U.K.
‡Royal College of Physicians, St Andrew’s Place, Regent’s Park, London NW1 4LE, U.K.
Recommended treatments

• Topical corticosteroids or topical calcineurin inhibitors

• Narrow-band UVB better than PUVA
Some definitions

The concept of targeted repigmentation

Excimer laser treatment of vitiligo: the evidence

Future perspectives
Clinical studies on excimer laser in vitiligo (PubMed search 2001-2013)
Distribution of RCTs on excimer laser in vitiligo by study focus (PubMed search 2001-2013)

![Bar chart showing distribution of RCTs]

- vs traditional UVB: 2 RCTs
- vs excimer light: 2 RCTs
- combination*: 5 RCTs
- frequency regimen: 1 RCT

* Combination regimens included: topical steroid (1), tacrolimus (2), pimecrolimus (1), calcipotriol (1)
Distribution of RCTs on excimer laser in vitiligo by study design (PubMed search 2001-2013)

Within patient control: 8
Parallel group: 2
Sample size in the RCTs analysed (PubMed search 2001-2013)
Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck

F. Sassi,* S. Cazzaniga,† G. Tessari,‡ L. Chatenoud,§ A. Reseghetti,¶ L. Marchesi,‖ G. Girolomoni‡ and L. Naldi*¶

*Centro Studi GISED and †Department of Dermatology, Ospedali Riuniti, 24100 Bergamo, Italy
†Department of Mathematics, University of Milan, Italy
‡Department of Dermatology, University of Verona, Italy
§Unit of Analytic Epidemiology, Mario Negri Institute for Pharmacological Research, Milan, Italy

British Journal of Dermatology 2008 159, pp1186–1191
Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck

F. Sassi,* S. Cazzaniga,*† G. Tessari,‡ L. Chatenoud,§ A. Reseghetti,¶ L. Marchesi,¶ G. Girolomoni‡ and L. Naldi*¶

**Study design**: parallel group randomised trial

**Treatment arms**: excimer laser vs excimer laser plus topical steroids

**Inclusion criteria**: stable vitiligo on the face or neck

**Sample size**: 84 patients

**Outcome measures**: repigmentation as assessed on UV-light reflected photographs
Physician's Global Assessment (PGA)
Skindex-29 scores variations
Entry criteria

- Age 18-75 years
- Vitiligo present since at least 6 months
- Lesions on the face and/or neck, exclusion of segmental vitiligo
- Lack of response to UVB or PUVA (at least 16 weeks of continuous treatment)
- Withdrawal of any topical agent since at least 15 days
Assessed for eligibility
(n = 102)

Excluded (n = 18)
Not meeting inclusion criteria (n = 16)
Refused to participate (n = 2)

Randomized (n = 84)

Allocated to laser monotherapy (n = 42)
Received allocated intervention (n = 42)

Discontinued intervention (n = 6)
Withdrew consent (n = 3)
Side-effects (n = 2)
Noncompliance (n = 1)

Analysed (n = 36)

Allocated to combined laser plus topical steroid (n = 42)
Received allocated intervention (n = 42)

Discontinued intervention (n = 2)
Withdrew consent (n = 2)

Analysed (n = 40)
Quality of life

Quality of life indices improved to a similar extent in the two treatment groups. The values of the composite score at entry were 19 ± 2 (SEM 2 ± 3) in the laser monotherapy group and 23 ± 1 (SEM 2 ± 8) in the combination group. At the end of the treatment course, values decreased to 14 ± 2 (SEM 2 ± 5) and 18 ± 7 (SEM 2 ± 8), respectively (Mann–Whitney U-test for between-group comparison, P = 0.27).

No significant differences were found between groups for any of the Skindex-29 subscales. Overall, variations were ) 0 ± 0 (SEM 1 ± 2) for symptoms, ) 7 ± 1 (SEM 1 ± 2) for emotion, and ) 2 ± 8 (SEM 0 ± 7) for social functioning subscales.
Prediction of Clinical Response to Excimer Laser Treatment in Vitiligo by Using Neural Network Models

Simone Cazzaniga\textsuperscript{a}  Fabrizia Sassi\textsuperscript{a}  Santo Raffaele Mercuri\textsuperscript{b}  Luigi Naldi\textsuperscript{a,c}
Risposta terapia vitiligine

**Parametri clinici**

- Dimensione lesione: [3% 17%]
- Sede: Lati viso
- Trattamento con cortisone: Sì
- Sesso: M
- Età: 30
- Altezza (cm): 175
- Colore occhi: Scuro
- Colore capelli: Scuro
- Fototipo: Abbastanza...
- Consumo alcolici: No
- Fumatore: No
- Parenti con vitiligine: No
- N° anni insorgenza generale: 15
- N° anni insorgenza sede: 10
- Tipologia vitiligine: Generalizz...
- Malattie autoimmuni: No

**Calcola**

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<th>N° sedute</th>
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<tr>
<td>75</td>
<td>29 [20 - 41]</td>
</tr>
<tr>
<td>100</td>
<td>38 [26 - 55]</td>
</tr>
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</table>

**Nome paziente:**

Nome paziente: [ ]

**Gráfico:**

![Gráfico de dos datos](image.png)

**Ejes:**

- Eje X: Ripigmentazione %
- Eje Y: N° sedute


• Single-blinded, randomized trial
• 308-nm excimer laser therapy plus topical 1% pimecrolimus cream twice daily (group A) vs excimer laser therapy twice per week alone (group B)
• Forty-nine patients enrolled, and 48 patients evaluated
• After 30 weeks of treatment, 71% of patients from group A achieved Grade 3 or 4 repigmentation compared with 50% in group B (p = 0.001).
Topical Tacrolimus and the 308-nm Excimer Laser

A Synergistic Combination for the Treatment of Vitiligo

Thierry Passeron, MD; Nima Ostovari, MD; Wassim Zakaria, MD; Eric Fontas, MD; Jean-Claude Larrouy, MD; Jean-Philippe Lacour, MD; Jean-Paul Ortonne, MD

Arch Dermatol. 2004;140:1065-1069

Forteen patients 4-10 target lesions per patient

Within patient control

Group A: combination of 308-nm excimer laser and 0.1% tacrolimus

Group B: 308-nm excimer laser monotherapy.

• Within patient control study

• Ten patients with vitiligo with bilateral symmetrical lesions

• All patients received 308-nm XeCl excimer laser therapy three times weekly. Calcipotriol ointment was applied to lesions on one side of the body twice daily.

• After 24 treatments (8 weeks), nine patients were evaluated. Eight patients showed evidence of repigmentation on both body sides, with no significant difference
A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients

M.W. Linthorst Homan,†,‡ Ph. I. Spuls,‡ L. Nieuweboer-Krobotova,†,‡ J. de Korte,‡ M.A.G. Sprangers,§ J.D. Bos,‡ A. Wolkerstorfer,†,‡ J.P.W. van der Veen†,‡,*

JEADV 2012, 26, 690–695
Study design: within patient control study

Treatment arms: excimer laser vs NB UVB after skin grafting

Inclusion criteria: symmetrical vitiligo patches on extremities

Sample size: 16 (lost to follow-up 2)

Outcome measures: repigmentation as assessed on photographs by image analysis patient satisfaction and patient preferences
A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients

M.W. Linthorst Homan,†,‡ Ph. I. Spuls,‡ L. Nieuweboer-Krobotova,†,‡ J. de Korte,‡ M.A.G. Sprangers,§ J.D. Bos,‡ A. Wolkerstorfer,†,‡ J.P.W. van der Veen†,‡,*

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<th>Repigmentation after excimer laser (%)</th>
<th>Repigmentation after NB-UVB (%)</th>
<th>Cumulative doses EL (J/cm²)</th>
<th>Cumulative doses NB-UVB (J/cm²)</th>
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Mean (SD) | 7.32 (3.50) | 25.60 (11.62) | 18.27 (8.34) |
A randomized within patient control trial

Fourteen subjects with 48 symmetrical vitiligo lesions were enrolled

One lesion was treated with the 308-nm excimer laser, and its counterpart was treated with the 308-nm excimer lamp.

Lesions were treated three times a week with the same dose on both sides for a total of 20 sessions.
Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study

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Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study
Within patient control study of 14 patients

Each patient had at least three stable vitiligo lesions in the same body area. The three stable vitiligo lesions in each subject were randomly assigned to receive excimer laser treatment once, twice, and three times weekly.

The initial ultraviolet (UV) dose was 50 mJ per square centimeter. The UV dose was increased at each treatment session according to the erythematous response to the previous treatment.

Thirteen subjects were treated for at least 6 weeks; seven were treated for all 12 weeks.
Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients

Lesions with no repigmentation vs. Number of treatments

Lesions with no repigmentation vs. Treatment time (weeks)

Treatment frequency per week:
- ▲ 1x
- ● 2x
- ■ 3x
Summary of the evidence

- Excimer laser may represent an option as a targeted therapy of vitiligo in photosensitive areas (face, neck).

- There is no indication that excimer laser is superior to targeted NB-UVB or excimer lamp.

- Combination with topical steroids (or calcineurin inhibitors) offers better results than excimer laser alone.

- Excimer laser achieves clinical response with less cumulative UV dose than NB-UVB.

- There is an obvious need to improve study quality.
• Some definitions
• The concept of targeted repigmentation
• Excimer laser treatment of vitiligo: the evidence
• Future perspectives
Pragmatic trials (1)

• Targeted therapy vs nontargeted therapy (total body NB-UVB vs excimer laser on limited areas)
• Combination therapies (topical steroids, ORS melanocytes)
• Home therapy vs hospital-based therapies (with excimer lamp)
• Early treatment
Pragmatic trials (2)

• Adequate time frame to assess persistence of response and relapse rates
• Outcome: patient preferences and quality of life
• Sample size issue and negative results
• Combination with epidemiologic approaches: assessment of predictors of response
study period

disease activity

time
Drawbacks of within patient control studies

- Cumbersome
- Not realistic manouvres, artificial conditions
- Problems with withdrawals
- Only short term assessment
Vitiligo Care concept

- Census of therapeutic offer in the country
- Definition of standards of care
- Establishment of a disease network with reference centres
- Development of RCTs, outcome studies and monitoring of quality of care
UNITED COLORS OF VITILIGO