Title: Therapeutic targets in the management of striae distensae: A systematic review

Article Type: Review

Keywords: striae distensae; striae rubrae; striae albae; stretch marks; therapy; treatment; management; systematic review.

Corresponding Author: Dr Ardeshir Bayat, MD PhD
Corresponding Author's Institution: University of Manchester
First Author: Adam Hague, MBChB, MRes
Order of Authors: Adam Hague, MBChB, MRes; Ardeshir Bayat, BSc, MBBS, MRCS, PhD

Abstract: Background: Striae distensae are permanent dermal lesions that can cause significant psychosocial distress. A detailed understanding of the numerous treatment modalities available is essential to ensuring optimal patient outcomes.

Objective: To evaluate and summarize the different treatment methods for striae distensae, by linking their proposed modes of action with the histopathogenesis of the condition, in order to guide patient management.

Methods: A systematic review of the literature was performed with no limits placed on publication date. Relevant studies were assigned a level of evidence by the authors.

Results: 92 articles were identified, with 74 being eligible for quality assessment. The majority of treatments aim to increase collagen production. The use of vascular lasers can reduce erythema in striae rubrae by targeting hemoglobin, whilst increasing melanin, through methods such as UV light, is a major focus for treatment of striae albae. Despite some topical treatments being widely used, uncertainty regarding their mode of action remains. No treatment has proven to be completely efficacious.

Limitations: Low quality evidence, small sample sizes, and varying treatment protocols and outcome measures limit our findings, along with concerns regarding publication bias.

Conclusions: Further randomized controlled trials are needed before definitive conclusions and recommendations can be made.
Dear Editor,

Thank you for accepting our systematic review for publication in JAAD, as well as providing us with suggestions for improvement regarding our tables. Please find below our response to these comments, along with a description of the changes that have subsequently been made in the revised manuscript and highlighted.

We look forward to hearing from you.

Yours sincerely,

Dr. Ardeshir Bayat
Editors comments

1. “JAAD is on a strict page budget. Tables 1, 2, and 3 are far too long to run in the print JAAD and can run online only and will be referenced with a link in the print JAAD. The online version of JAAD (which will contain all the tables) is the official archived version of the journal which is accessed by anyone doing a literature search (PubMed, etc.).

Please rename Tables 1, 2 and 3 as Supplementary Tables 1, 2 and 3 and make the same changes to their citations in the text.

Table IV (which will run the print JAAD) should be renamed Table 1; please make the same change to its citation in the text.” – Thank you for informing us of this. Tables I, II and III have been renamed as Supplemental Table II, III and IV respectively (Supplemental Table I outlining our quality rating scheme remains the same). Table IV has now been renamed Table I. Changes to their citations in the text have also been made.

2. “Regarding current Table IV, it seems that tretinoin fits into both categories, which is a bit awkward. Please insert a footnote explaining that different studies came to opposite conclusions.” – Thank you for this suggestion. Table I (previously Table IV) has now been amended accordingly.
Therapeutic targets in the management of striae distensae: A systematic review

Authors:

1. Adam Hague MBChB (Hons), MRes
2. Ardeshir Bayat BSc (Hons), MBBS, MRCS (Eng, Edin), PhD

Affiliation:
Centre for Dermatological Research, University of Manchester, Manchester, England, UK.

Correspondence:
Dr. Ardeshir Bayat, Centre for Dermatological Research, University of Manchester, Oxford Road, Manchester, M13 9PT, England, UK.
Email: ardeshir.bayat@manchester.ac.uk  Tel: +44 (0)161 306 0607

Abstract word count: 200
Capsule summary word count: 49
Article word count: 2498
Figure count: 3
Table count: 1
Supplementary table count: 4
Reference count: 106

Funding sources: none
The authors have no conflicts of interest to disclose.
Capsule Summary

- Striae distensae are extremely common, permanent dermal lesions. There is great demand for an effective treatment option.
- The majority of treatments aim to increase collagen production, reduce erythema or increase pigmentation.
- Despite some positive outcomes, definitive recommendations cannot yet be made due to a lack of high quality evidence.
Abstract

Background: Striae distensae are permanent dermal lesions that can cause significant psychosocial distress. A detailed understanding of the numerous treatment modalities available is essential to ensuring optimal patient outcomes.

Objective: To evaluate and summarize the different treatment methods for striae distensae, by linking their proposed modes of action with the histopathogenesis of the condition, in order to guide patient management.

Methods: A systematic review of the literature was performed with no limits placed on publication date. Relevant studies were assigned a level of evidence by the authors.

Results: 92 articles were identified, with 74 being eligible for quality assessment. The majority of treatments aim to increase collagen production. The use of vascular lasers can reduce erythema in striae rubrae by targeting hemoglobin, whilst increasing melanin, through methods such as UV light, is a major focus for treatment of striae albae. Despite some topical treatments being widely used, uncertainty regarding their mode of action remains. No treatment has proven to be completely efficacious.

Limitations: Low quality evidence, small sample sizes, and varying treatment protocols and outcome measures limit our findings, along with concerns regarding publication bias.

Conclusions: Further randomized controlled trials are needed before definitive conclusions and recommendations can be made.
Keywords: striae distensae, striae rubrae, striae albae, stretch marks, therapy, treatment, management, systematic review.
Introduction

Striae distensae (SD), also known as stretch marks, are common, permanent dermal lesions that can be symptomatic, and are considered aesthetically undesirable. Thus, they pose a significant psychosocial and therapeutic challenge. They arise in areas of dermal stretching and most commonly occur on the abdomen, breasts, buttocks and thighs.\textsuperscript{1-3} Most literature has described SD during pregnancy (striae gravidarum) and puberty, with reported prevalences varying from 11-88\%.\textsuperscript{1,2,4-7} Hormonal influences,\textsuperscript{8-12} reduced genetic expression of fibronectin, collagen and elastin,\textsuperscript{13,14} along with mechanical stretching of the skin,\textsuperscript{2,15-17} have all been postulated to contribute to SD formation. In the acute phase, SD present as red/violaceous lesions (striae rubrae; SR) that can be raised and symptomatic.\textsuperscript{18} The chronic form (striae albae; SA) exists as hypopigmented dermal depressions.\textsuperscript{18,19}

Because of their high prevalence and impact on patients’ quality of life,\textsuperscript{20} there is great demand for an effective treatment. A vast array of treatment modalities have been investigated, ranging from topicals\textsuperscript{19} and acid peel treatments,\textsuperscript{21} to more invasive methods such as laser therapy.\textsuperscript{22} Although completely eradicating SD is not attainable, improving appearance whilst reducing physical symptoms certainly is. It is therefore essential that clinicians managing SD have a detailed understanding of available treatment strategies in order to optimize patient outcomes and expectations.
We herein present a systematic review of SD focusing on the different treatments and their proposed modes of action with outcomes, in relation to the histopathogenesis of the condition.

**Methods**

Searches of both PubMed/Medline and Scopus were conducted using the keywords “stretch marks”, “striae distensae”, “striae rubra”, “striae alba”, “striae gravidarum”, AND “management”, OR “treatment”. No limits were placed on publication date, with the last literature search being conducted in November 2016. Citations of articles were also reviewed. Exclusion criteria consisted of animal/in vitro studies, non-English articles, unavailability of full text, book chapters, conference papers, letters, and reviews not specific to SD.

Data including treatment protocols, number of participants, and striae type were extracted. Relevant articles were assigned a level of evidence (LOE) independently by the authors based on a quality rating scheme modified from the Oxford Centre for Evidence-Based Medicine for ratings of individual studies (Supplemental Table I). The risk of bias was assessed for at both study and outcome level.

**Results**

92 articles of the 383 initially identified were included for analysis (Figure 1). 74 publications, representing 2328 patients, were relevant for quality
assessment and assigned a LOE, the results of which are as follows: level 1, 15 (20.3%); level 2, 31 (41.8%); level 4, 28 (37.8%).

**Histopathogenesis**

SD were first histologically described in 1889,\(^23\) with SR and SA being histologically distinct from one another (Figure 2).\(^{24-32}\) They exhibit abnormalities in three core components of skin which normally provide it with tensile strength and elasticity; collagen, elastin and fibrillin.\(^{25-29}\) Early changes associated with SR include accumulation of degranulating mast cells and macrophages around mid-dermal elastic fibers, resulting in elastolysis.\(^{24}\)

These changes may be seen in macroscopically normal skin up to 3cm away from the lesion.\(^{24}\) As the striae progress to form SA, there is gradual epidermal atrophy with loss of rete ridges.\(^{24,25}\)

**Treatment**

Enhanced collagen production (*Supplemental Table II*)

The vast majority of treatments are targeted towards stimulating collagen production (Figure 3).

**Topical agents**

Tretinoin (retinoic acid) is believed to increase tissue collagen I levels through stimulation of fibroblasts,\(^{19,33}\) and has also inhibited activation of matrix-degrading enzymes following ultraviolet (UV) induced skin damage, implying it may also protect the skin from other mechanisms of injury.\(^{19}\) Numerous studies, have investigated its efficacy (LOE 1,2,4),\(^{33,34-37}\) with the majority
suggesting that it can improve the appearance of early SD but not at lower doses. However, study populations were small and common side effects included transient erythema and scaling of the skin.

Centella asiatica is a plant used in Asian herbal medicine. It contains asiaticoside which stimulates fibroblasts, with antagonistic effects on glucocorticoids also described. Its use in the prevention of striae gravidarum has been investigated, with reported reductions in the development and severity of striae (LOE 1). No side effects were observed. The use of Centella asiatica combined with boswellic acid, previously found to have anti-inflammatory effects, has also been tested. Reductions in striae severity were noted, however side effects included pruritus (LOE 4).

Hyaluronic acid is also thought to increase collagen production through stimulation of fibroblasts. Two RCTs (LOE 1) have reported improvements in the appearance of striae following its use, with a reported side effect being pain following treatment. No follow up was conducted and both incorporated subjective assessments into their outcome measures.

Chemical peel treatments

Chemical peel treatments involve the application of trichloroacetic acid (TCA) or glycolic acid (GCA). They are thought to induce an initial inflammatory response, with subsequent increased collagen production. A nonrandomized controlled trial investigating GCA reported decreases in striae furrow width, however concluded it may yield better results when used in
combination with other products. GCA combined with tretinoin and L-ascorbic acid, and TCA combined with the use of sand abrasion or a postpeel cream are such examples, all of which produced improvements in the appearance of striae. No RCTs have been performed (GCA – LOE 2, TCA – LOE 4) and postinflammatory hyperpigmentation (PIH) remains a concern.

Mechanical techniques

Aluminum oxide microdermabrasion mechanically ablates damaged skin. A study investigating its use in SD reported clinical improvements and increased type 1 procollagen formation (LOE 2). Reported side effects included PIH.

Radiofrequency (RF) devices

RF devices deliver RF current to the skin, which is converted to heat in the dermis due to its electrical resistance. Following initial collagen denaturation with its use, there is subsequent increased collagen production. The majority of trials investigating RF for the treatment of SD have reported clinical improvements (LOE 1,2,4). However, side effects include erythema and edema, and the majority of trials had small cohorts.

Fractional lasers

Fractional lasers deliver microscopic beams of coherent and monochromatic light energy to the skin, creating areas of thermal damage termed
microthermal zones, leading to increased dermal collagen production.\textsuperscript{53-56} Both ablative and non-ablative lasers are available, with ablative lasers targeting water and resulting in cell vaporization.\textsuperscript{53} Improvements in SD following treatment with a 1540-nm fractional non-ablative erbium glass (Er:glass) laser have been reported (LOE 1,2,4).\textsuperscript{55-60} Malekzad et al\textsuperscript{61} however, observed only a fair or poor improvement in 70% of patients with its use (LOE 4), and although improvements in SR have been described (LOE 4),\textsuperscript{62-64} the literature suggests that non-ablative lasers are most effective on SA (LOE 4).\textsuperscript{57} Concerns surrounding PIH also remain.\textsuperscript{18,57,61,63}

Fractional ablative CO\textsubscript{2} lasers have primarily been utilized in SA, with reported clinical improvements (LOE 2,4).\textsuperscript{65-69} Side effects include PIH. Gungor et al\textsuperscript{70} compared the efficacy of an ablative erbium-yttrium aluminum garnet (Er:YAG) laser with a non-ablative neodymium-doped yttrium aluminum garnet (Nd:YAG) laser and found poor clinical results with both (LOE 2). When compared to non-ablative lasers, the literature suggests ablative lasers are less well tolerated and produce inconsistent results.\textsuperscript{53}

\textit{Diode laser}

The 1450-nm diode laser is a non-fractional laser, which has been shown to increase dermal collagen.\textsuperscript{71} However, a RCT investigating its use in Fitzpatrick skin types IV-VI reported no improvements in SD, but high rates of PIH (LOE 1).\textsuperscript{71}
**Intense pulsed light (IPL)**

IPL consists of a broad-spectrum (515-1200-nm) visible beam of high intensity light. Studies investigating its use in SD have demonstrated increased dermal collagen levels following treatment (LOE 4). However, a study comparing IPL against a fractional CO₂ laser for the treatment of SD, concluded that the laser was more effective (LOE 2). No RCTs have yet been performed and PIH remains a cause for concern.

**Percutaneous collagen induction therapy (PCT)**

PCT, or needling therapy, involves the creation of micro-clefts extending to the papillary dermis, resulting in increased production of collagen and elastin. Aust et al reported improvements in skin texture and tightening following treatment (LOE 4). More recently, PCT compared favorably against microdermabrasion combined with sonophoresis, and a CO₂ laser (LOE 2). However, there are no RCTs, and side effects include erythema.

**Platelet-rich plasma (PRP)**

PRP is a concentrated solution of autologous platelets containing growth factors and cytokines injected intradermally. Ibrahim et al investigated its use in SD with microdermabrasion, and despite increased collagen levels following PRP treatment alone, 13% developed worsening of their striae (LOE 2). They concluded it is best to use PRP in combination with microdermabrasion. Other studies have combined PRP with RF (LOE 4) and microneedling (LOE 2), all reporting varying degrees of clinical
improvement. However, small sample sizes and no RCTs make drawing definitive conclusions difficult. Side effects include bruising. Infrared light

Infrared light applied to skin causes heating of the dermis and collagen denaturation, with subsequent neocollagenesis. Trelles et al investigated its use in the treatment of SA. Despite positive histological findings, including more pronounced rete processes, detection of improvements clinically remained low (LOE 4). Side effects were limited to erythema of the skin.

Galvanopuncture

Galvanopuncture is a needling therapy which applies a continuous microcurrent, inducing an inflammatory reaction with subsequent collagen production. Bitencourt et al investigated its use in SA. All patients demonstrated clinical improvements and erythema was the only side effect (LOE 4). Further trials, with histological analysis, are needed to further assess its efficacy.

Reduced vascularity (Supplemental Table III)

Vascular lasers

The 585-nm pulsed dye laser (PDL) is a commonly used vascular laser. Due to its high affinity for hemoglobin, which is present in the microvasculature of SR, it can reduce the erythema of these lesions (LOE 2). Although improvements in both collagen and elastin been described following PDL treatment, these are probably subclinical and PDL is likely to have minimal
benefit in the treatment of SA (LOE 2,4). Care should be taken when using PDL with darker skin types (Fitzpatrick IV to VI), as melanin competes with hemoglobin for the light energy, which can result in PIH. Longo et al. tested the 577-nm copper bromide laser, which has higher rates of absorption by hemoglobin than its PDL counterpart. 33% had complete resolution of their SD with the remainder showing a reduction in striae size (LOE 4). Crusting of the skin was a reported side effect. The Nd:YAG vascular laser has also produced clinical improvements in SR (LOE 2,4), however side effects include PIH.

Increased melanin (Supplemental Table IV)

UV light

A major aim for the treatment of SA is repigmentation of the lesion. Sadick et al. investigated the combined use of UVB (296-315-nm) and UVA1 (360-370-nm) light in nine individuals. Despite all patients initially having >50% improvement in pigmentation, this was only temporary and side effects included transient hyperpigmentation (LOE 2).

Excimer laser

The xenon chloride (XeCl) excimer laser delivers narrow band (308-nm) UVB radiation. Its proposed advantages include being able to deliver the radiation quicker with increased precision when compared with standard UV therapy. Studies have reported improvements in striae pigmentation following its use (LOE 1,4). However, poor results were observed elsewhere (LOE 2) and...
splaying of the pigment to involve surrounding skin is a reported side
effect.\textsuperscript{93,95}

A study investigating UVB light therapy and the XeCl excimer laser found that
both cause hypertrophy and increase of melanocytes, along with an increase
in melanin, albeit not permanent.\textsuperscript{96}

Other (Supplemental Table IV)

Bio-Oil\textsuperscript{®} (Union Swiss Ltd, South Africa) consists of vitamins and plant
extracts with an oil base.\textsuperscript{97} One study investigating its use in SD
demonstrated visual improvements after two weeks (LOE 2).\textsuperscript{98} No side effects
were reported.

Cocoa butter is a natural fat, and used as a topical formulation to rehydrate
the skin.\textsuperscript{99} Two trials have investigated its use in preventing SD (LOE 1).\textsuperscript{100,101}
Both failed to show any significant benefits with its use.

Soltanipoor et al\textsuperscript{102} and Taavoni et al\textsuperscript{103} hypothesized that, because of its high
vitamin E content and moisturizing properties, olive oil could have a role in
preventing striae gravidarum. However, no benefits with its use were reported
(LOE 1).

Taşhan et al\textsuperscript{104} studied the use of almond oil alone and with massage in
preventing striae gravidarum formation, and observed fewest striae in those
applying almond oil with massage (LOE 2). However, a RCT comparing the
effects of an Iranian produced cream (Saj®, Seoidrood Co, Iran), containing almond oil, against olive oil, found neither were effective at reducing severity of striae gravidarum (LOE 1).\textsuperscript{105} No side effects were reported in either trial.

Silicone gel has previously been used to improve scars, with promoting skin hydration being one proposed mode of action\textsuperscript{106} Ud-din et al\textsuperscript{106} investigated the effect of silicone against a placebo on SD. They demonstrated increased melanin and decreases in hemoglobin and collagen with both gels. They concluded that the application of gels by topical massage can improve SD (LOE 1). No side effects were reported.

Discussion
SD are common yet undesirable permanent dermal lesions. Despite a basic understanding of the etiology and histopathological changes that occur, finding an effective treatment is proving challenging. The majority of treatment modalities are targeted towards increasing collagen production. Topical treatments in this category still lack consistent high quality evidence, with the effects of massage potentially influencing the findings. Tretinoin has had variable outcomes, with its efficacy mostly demonstrated for the treatment of SR, and despite both Centella asiatica and hyaluronic acid yielding promising results (Table I), uncertainty regarding the type of striae they are most effective against remains. Chemical peel treatments, microdermabrasion, PRP and PCT also lack high quality evidence, with no RCTs having yet been performed. Emerging techniques such as galvanopuncture look promising, however knowledge regarding its mode of action specific to SD is lacking,
Lasers have been used in attempts to increase collagen production, reduce erythema in SR, and increase pigmentation in SA. Accurately interpreting these studies is difficult, owing to the small sample sizes used and short follow up periods. UV light has shown promise for the repigmentation of SA, although its lack of permanency means repeated sessions would be needed. Numerous other topicals, which mostly claim to hold moisturizing properties, are widely marketed despite lack of evidence regarding their mode of action or efficacy.

Limitations

Exclusion criteria used may have resulted in relevant studies being missed, if for example they were not published in the English language. Of those included making direct comparisons is extremely difficult, even for those using the same treatment modality, due to widely varying treatment protocols and differences in study populations. This is compounded by the different outcome measures utilized, of which none are yet validated. A large proportion assessed for improvements through the use of clinical photographs, with differences in lighting potentially influencing results. Patient satisfaction scores were also widely used, however one may question whether scores would change if the treatments were not free/provided outside the trial setting. Small sample sizes and limited follow up periods are also major limitations in a large proportion of studies. Concerns surrounding publication bias also remain, as the vast majority of papers reported some positive results.
Conclusion

Further RCTs are needed before definitive conclusions and recommendations can be made. Future work should focus on creating standardized outcome measures and treatment protocols in order to enable accurate comparisons between treatments.

Acknowledgements

We would like to thank Helen Carruthers for producing the figure illustrations. No external funding was received and we have no conflicts of interest to disclose.
Abbreviations used

SD, striae distensae; SR, striae rubrae; SA, striae albae; LOE, level of evidence; UV, ultraviolet; RCT, randomized controlled trial; TCA, trichloroacetic acid; GCA, glycolic acid; PIH, postinflammatory hyperpigmentation; RF, radiofrequency; Er:glass, erbium glass; Er:YAG, erbium-yttrium aluminum garnet; Nd:YAG, neodymium-doped yttrium aluminum garnet; IPL, intense pulsed light; PCT, percutaneous collagen induction therapy; PRP, platelet-rich plasma; PDL, pulsed dye laser; XeCl, xenon chloride.
References:


20. Yamaguchi K, Suganuma N, Ohashi K. Quality of life evaluation in Japanese pregnant women with striae gravidarum: a cross sectional...


30. Denvillers C, Piérard-Franchimont C, Schreder A, Docquier V, Piérard GE. High resolution skin colorimetry, strain mapping and


68. Naeini FF, Behfar S, Abtahi-Naeini B, Keyvan S, Pourazizi M. Promising option for treatment of striae alba: fractionated


90. Nouri K, Romagosa R, Chartier T, Bowes L, Spencer JM. Comparison of the 585 nm pulsed dye laser and the short pulsed CO2 laser in the


Figure 1: Flow diagram outlining article selection.

Figure 2: Striae Distensae. Histological differences between normal skin (a), striae rubrae (b), and striae albae (c).

Haematoxylin and eosin stain. a) Small collagen bundles and elastin fibers gradually increase in thickness towards deeper areas of the dermis.\(^{32}\) b) Perivascular lymphocyte cuffing along with dermal edema and an increase in glycosaminoglycans may be observed.\(^{25,27,30,53}\) c) Collagen fibers are stretched, aligned parallel to the dermal-epidermal junction and a scanty lymphocytic infiltrate predominates.\(^{25-28,32,53}\)

Figure 3: Treatments for SD and the highest LOE available for their use.

The majority of treatments are targeted towards enhancing collagen production. A large proportion of the RCTs conducted have been with topical agents, producing varying results. (LOE – level of evidence, TCA - trichloroacetic acid, GCA – glycolic acid, RF – radiofrequency, IPL – intense pulsed light, PCT – percutaneous collagen induction therapy, PRP – platelet-rich plasma, PDL – pulsed dye laser, Nd:YAG - neodymium-doped yttrium aluminum garnet, UV – ultraviolet, XeCl – xenon chloride).
133 Records identified through PubMed/MEDLINE

250 Records identified through Scopus

53 Duplicate records removed

330 Records screened by title/abstract

246 Records excluded:
- Animal studies/in vitro, non-English, full text not available, book chapters, letters, conference papers, irrelevant, reviews not specific to SD

84 Full-text articles assessed for eligibility

11 Articles identified by reference screening

3 Articles excluded:
- Irrelevant, reviews not specific to SD

92 Articles included in synthesis
Figure (.jpg, .eps. or .tif format ONLY)
Click here to download high resolution image

**Normal Skin**
- Visible downward epidermal projections (rete ridges)
- Thin, randomly arranged collagen and elastin fibers in the papillary dermis
- Thick collagen bundles predominate in the reticular dermis

**Striae Rubrae**
- Predominance of fine dermal elastic fibers with evidence of structural changes in collagen
- Dermal edema
- Increased microvasculature contributing to their erythematous color

**Striae Albae**
- Epidermal atrophy with loss of rete ridges
- Densely packed collagen fibers aligned parallel to dermal-epidermal junction
- Elastic fibers arranged in a similar pattern to those of collagen
- Reduced microvasculature resulting in their pale color
Treatment of striae distensae

Modes of action

Enhanced collagen production
- Topicals:
  - Retinoic acid (LOE 1)\(^{1,2,3,4}\)
  - Centella asiatica (LOE 1)\(^{5,6}\)
  - Hyaluronic acid (LOE 1)\(^{7,8}\)
- Chemical peels:
  - TCA (LOE 4)\(^{9,10}\)
  - GCA (LOE 2)\(^{11,12}\)
- Fractional lasers:
  - Ablative (LOE 2)\(^{13,14,15}\)
  - Non-ablative (LOE 1)\(^{16}\)
- Mechanical techniques:
  - Microdermabrasion (LOE 2)\(^{6,7}\)

Reduced vascularity
- Vascular lasers:
  - PDL (LOE 2)\(^{17,18,19}\)
  - Copper bromide laser (LOE 4)\(^{20}\)
  - Nd:YAG laser (LOE 2)\(^{21,22}\)
- UV light:
  - UVB/UVA1 (LOE 2)\(^{23}\)
- Laser light:
  - XeCl excimer laser (LOE 1)\(^{24}\)

Increased melanin
- Topical agents:
  - Bio-oil (LOE 2)\(^{25}\)
  - Cocoa butter (LOE 1)\(^{26,27}\)
  - Olive oil (LOE 1)\(^{28,29}\)
  - Almond oil (LOE 1)\(^{30}\)
  - Silicone gel (LOE 1)\(^{31}\)

Other
- Other:
  - RF (LOE 1)\(^{32}\)
  - Diode laser (LOE 1)\(^{33}\)
  - IPL (LOE 2)\(^{16,20,34}\)
  - PCT (LOE 2)\(^{35,36,37}\)
  - PRP (LOE 2)\(^{38}\)
  - Infrared light (LOE 4)\(^{39}\)
  - Galvanopuncture (LOE 4)\(^{40}\)
**Table I:** Treatment modalities with level 1 evidence supporting their efficacy and/or ineffectiveness.

<table>
<thead>
<tr>
<th>Effective</th>
<th>Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tretinoin*19,33</td>
<td>Tretinoin*35</td>
</tr>
<tr>
<td>Centella asiatica38,40</td>
<td>Non-fractional diode laser71</td>
</tr>
<tr>
<td>Hyaluronic acid40,41</td>
<td>Cocoa butter100,101</td>
</tr>
<tr>
<td>Radiofrequency49</td>
<td>Olive oil102,103,105</td>
</tr>
<tr>
<td>Fractional erbium glass laser56</td>
<td>Almond oil105</td>
</tr>
<tr>
<td>Xenon chloride excimer laser94</td>
<td>Silicone gel106</td>
</tr>
</tbody>
</table>

*Separate studies came to opposite conclusions*
**Supplemental Table I:** Quality rating scheme modified from the Oxford Centre for Evidence-Based Medicine for ratings of individual studies.

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td></td>
<td>Systematic review with meta-analysis</td>
</tr>
<tr>
<td>2</td>
<td>Nonrandomized controlled trial</td>
</tr>
<tr>
<td></td>
<td>Prospective comparative cohort trial</td>
</tr>
<tr>
<td>3</td>
<td>Case-control study</td>
</tr>
<tr>
<td></td>
<td>Retrospective cohort study</td>
</tr>
<tr>
<td>4</td>
<td>Case series</td>
</tr>
<tr>
<td></td>
<td>Cross sectional study</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion</td>
</tr>
<tr>
<td></td>
<td>Case reports</td>
</tr>
</tbody>
</table>
**Supplemental Table II:** Summary and LOE for treatments used to enhance collagen production in SD.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Dosage/Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang et al(^{19,33})</td>
<td>Tretinoin cream vs. placebo</td>
<td>0.1% Daily for 6 months</td>
<td>SR</td>
<td>22 (10 treatment, 12 placebo)</td>
<td>Severity assessment scale: none, mild, moderate, severe Patient self assessment Striae length and width Histological analysis</td>
<td>47% reduction in mean severity score of treatment group vs. 2% increase in control 80% of treatment group had marked or definite improvement vs. 8% in control Reduction in length and width (14% and 8% respectively) in treatment group vs. increase (10% and 24% respectively) in control group No significant changes in dermal elastic or collagen fibers</td>
<td>Erythema Scaling Pruritus/burning sensation More common in first 2 months</td>
<td>1</td>
</tr>
<tr>
<td>Pribanich et al(^{35})</td>
<td>Tretinoin cream vs. placebo</td>
<td>0.025% Daily for 7 months</td>
<td>SR and SA</td>
<td>11 (6 treatment, 5 placebo)</td>
<td>Severity assessment scale: none, mild, moderate, moderate-severe, severe</td>
<td>No significant differences between treatment and control group</td>
<td>Pruritus</td>
<td>1</td>
</tr>
<tr>
<td>Rangel</td>
<td>Tretinoin</td>
<td>0.1%</td>
<td>Not</td>
<td>20</td>
<td>Overall response to 80% had marked to</td>
<td></td>
<td>Erythema and</td>
<td>2</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Duration</td>
<td>Baseline &amp; Treatment</td>
<td>Clinical Improvement</td>
<td>Histological Analysis</td>
<td>Side Effects</td>
<td>Results</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------------------</td>
<td>---------------------------</td>
<td>----------------------</td>
<td>----------------------</td>
<td>------------------------</td>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>et al^36</td>
<td>Tretinoin cream</td>
<td>Daily for 3 months</td>
<td>stated</td>
<td>Treatment: -1 = worse to 4 = cleared Striae length and width</td>
<td>Moderate global improvement Reduction in length and width by 20% and 23% respectively</td>
<td>Scaling in first month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elson^37</td>
<td>Tretinoin cream 0.1%</td>
<td>Daily for 3 months</td>
<td>Not stated</td>
<td>Striae observations during treatment (not otherwise specified)</td>
<td>15 patients experienced “some benefit” with treatment Some had complete clearing of lesions (no number given)</td>
<td>Erythema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hexsel et al^34</td>
<td>Tretinoin cream vs. superficial dermabrasion</td>
<td>0.05% Tretinoin – daily Dermabrasion - weekly Both for 16 weeks</td>
<td>SR</td>
<td>Global Aesthetic Improvement Scale: worse, no change, improved, much improved, very much improved Patient satisfaction: very unsatisfied, unsatisfied, neither satisfied nor unsatisfied, satisfied, very satisfied Length and width of striae Histological analysis</td>
<td>Clinical improvements in both groups but no significant differences between treatments Satisfaction scores (Tretinoin vs. dermabrasion): Neither satisfied nor unsatisfied 16.7% vs. 16.7%, satisfied 66.7% vs. 33.3%, very satisfied 16.7% vs. 50% Significant reductions in length and width of striae in both groups but no significant</td>
<td>Pruritus, Erythema Burning sensation, Scaling/crusting Pain Swelling Papules All present in both groups with no significant differences between treatments</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
differences between treatments
Reduction in elastolysis, collagen fragmentation and epidermal atrophy in dermabrasion group

| Mallol et al\textsuperscript{38} | Trofolastin (Centella asiatica, α-tocopherol, collagen-elastin hydrolisates) vs. placebo | Daily 12\textsuperscript{th} week of pregnancy to labor | Not stated | 80 (41 trofolastin, 39 placebo) | Presence of new striae and severity: 0 = no striae, 1 = few and thin, 2 = many thin or few thick, 3 = many thick | 34\% of treatment vs. 56\% of placebo group developed striae. Severity score was 1.42 in treatment vs. 2.13 in placebo group | None stated | 1 |

<p>| Sparavigna et al\textsuperscript{39} | Boswellic acid based cream with Centella asiatica, soia phospholipids and polyunsaturated fatty acids | Twice daily for 3 months to striae and forearm | Not stated | 113 | Severity score: Grade 1 = &lt; 10 lesions, &lt; 3 cm long and &lt; 5 mm thick, Grade 2 = &gt; 10 lesions, &lt; 3 cm long, and &lt; 5 mm thick, Grade 3 = &gt; 10 lesions, &gt; 3 cm long and &lt; 5 mm thick, Grade 4 = &gt; 10 lesions, &gt; 3 cm long and &gt;5 mm thick. Signs of erythema, | Mean global severity score reduced by 10% Significant mean improvements in erythema (46.1%), edema (35.3%) and atrophy (29.6%). Mean increase in skin extensibility at 90 days by 3% | Pruritus, Erythema, Burning | 4 |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Treatment Details</th>
<th>Control Details</th>
<th>Clinical Assessment Details</th>
<th>Skin Elasticity</th>
<th>Pain on Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Draelos et al&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Onion extract cream with Centella asiatica and hyaluronic acid</td>
<td>Twice daily for 12 weeks to thigh</td>
<td>SR 52</td>
<td>Clinical assessment by patient and investigator of softness, texture, color and appearance: 0 = no improvement, 1 = minimal improvement, 2 = mild improvement, 3 = moderate improvement, 4 = marked improvement</td>
<td>No significant improvements in skin elasticity</td>
<td>None stated</td>
</tr>
<tr>
<td>Morganti et al&lt;sup&gt;41&lt;/sup&gt;</td>
<td>Injectable + topical hyaluronic acid, betaglucan, vit C vs. topical application</td>
<td>Twice weekly dermal injections with twice daily application of topical agents for 16 weeks</td>
<td>Not stated</td>
<td>Prophilometry and reduction in color/overall appearance: 0 = normal color and dermatoglyphic pattern, 0.5 = white/pinky color</td>
<td>Use of treatment injection and topical provided superior results in all areas when compared to both other groups</td>
<td>Pain on injection 1</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Treatment Details</td>
<td>Clinical Appearance</td>
<td>Improvements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>------------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adatto and deprez&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Sand abrasion + TCA + post-peel cream (fatty acids, vit C,E,H, tretinoin precursors, algues and oligo-elements)</td>
<td>Clinical appearance: 1 = fresh, inflammatory, 2a = white, superficial without laddering and palpable depressions, 2b = white, without laddering but with palpable depressions, 3a = white, with laddering &lt;1cm width without deep pearliness, 3b = white, with laddering &lt;1cm width with deep pearliness, 4 = white with laddering &gt;1cm width +/- deep pearliness</td>
<td>70% average improvement in all types of striae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mazzare-GCA lotion</td>
<td>GCA lotion</td>
<td>70%</td>
<td>Skin anisotropy, Significant decrease in PIH particularly in darker skin types</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Follow-up</td>
<td>Evaluation Methods</td>
<td>Results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>-----------</td>
<td>--------------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ilo et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>vs. placebo 6 times over 6 months and SA</td>
<td></td>
<td>furrow width and number, hemoglobin and melanin content</td>
<td>furrow width and hemoglobin in SR Significant decrease in furrow width in SA with an increase in melanin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ash et al&lt;sup&gt;43&lt;/sup&gt;</td>
<td>GCA + L-ascorbic acid, zinc sulfate, tyrosine vs. GCA + Tretinoin</td>
<td>GCA – 20% Tretinoin – 0.05% Daily for 12 weeks to opposite sides of abdomen or thigh</td>
<td>SA 10</td>
<td>Clinical evaluation based on length, width and overall appearance Profilometry Histological analysis</td>
<td>Clinical improvements with both regimens but no differences between treatments No significant differences in profilometry measurements Tretinoin regimen increased reticular and papillary dermal elastin content Both increased epidermal thickness and decreased papillary dermal thickness Mild irritation and dermatitis with both treatments</td>
<td></td>
</tr>
<tr>
<td>Deprez&lt;sup&gt;44&lt;/sup&gt;</td>
<td>TCA based easy peel solution + post-peel cream</td>
<td>TCA – 50% Up to 8 treatments monthly</td>
<td>Not stated</td>
<td>50</td>
<td>Clinical appearance Depth of striae Almost all had a 60-75% improvement Reduced depth of striae (no further information given)</td>
<td>PIH</td>
</tr>
<tr>
<td>Ibrahim et al&lt;sup&gt;45&lt;/sup&gt;</td>
<td>Intradermal PRP (group 4-6 sessions at 2-week)</td>
<td>SR and 68 (23 group 1,</td>
<td>Clinical assessment of improvement: Significant clinical improvements with</td>
<td>Group 1 – pain on injection,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Interventions</td>
<td>Control</td>
<td>Clinical Assessment</td>
<td>Histological Analysis</td>
<td>Patient Satisfaction</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>---------------</td>
<td>---------</td>
<td>---------------------</td>
<td>-----------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Abdel-Latif and Elbendary&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Microdermabrasion</td>
<td>5 sessions at weekly intervals Other half of body acted as control</td>
<td>SR and SA</td>
<td>Clinical assessment of improvement: mild (&lt;25%), moderate (25-50%), good (50-75%), excellent (&gt;75%) Analysis of type 1 procollagen α1 mRNA levels</td>
<td>Good to excellent improvement in 50% and mild to moderate improvement in the rest Greater improvement in SR Increased type 1 procollagen α1 mRNA levels in treated striae</td>
<td>Patient satisfaction: not satisfied, slightly 25-50% and 51-75% improvement in 38.2% and 11.8% of patients respectively 12%, 23% and 65% of patients were slightly</td>
</tr>
<tr>
<td>Manuskiatti et al&lt;sup&gt;47&lt;/sup&gt;</td>
<td>TriPollar RF device</td>
<td>40-50 W 6 sessions with weekly intervals</td>
<td>SR and SA</td>
<td>Clinical assessment of improvement: &lt;25%, 25-50%, 51-75%, &gt;75% Patient satisfaction: not satisfied, slightly 25-50% and 51-75% improvement in 38.2% and 11.8% of patients respectively 12%, 23% and 65% of patients were slight</td>
<td>Ecchymosis, worsening of striae Group 2 – worsening of striae Group 3 – pain on injection, ecchymosis</td>
<td></td>
</tr>
</tbody>
</table>

1) vs. microdermabrasion (group 2) vs. intradermal PRP + microdermabrasion (group 3)
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Protocol Details</th>
<th>Outcome Measures</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suh et al⁴⁸</td>
<td>RF + PDL</td>
<td>3 sessions 4 weeks apart RF - 53-97 J/cm², PDL – 585-nm First session both PDL + RF were used Weeks 4+8 PDL alone was used</td>
<td>Satisfied, satisfied, extremely satisfied Striae surface smoothness Respective No significant differences in striae surface smoothness</td>
<td>Transient purpura PIH</td>
</tr>
<tr>
<td>Harmelin et al⁴⁹</td>
<td>Bipolar RF + IR light vs. fractional bipolar RF vs. fractional bipolar RF + bipolar RF + IR light</td>
<td>Bipolar RF + IR light - 100 J/cm², Fractional bipolar RF - 50-65 mJ/pin Monthly sessions for 3 months Abdomen</td>
<td>Depth and width of striae Global Assessment scale: -1 = worsening of lesion, 0 = no change, 1 = slight improvement, 2 = moderate improvement, 3 = Good improvement, 4 = Very good improvement</td>
<td>Bipolar RF – transient crusts, PIH Mild pruritus with all treatments</td>
</tr>
<tr>
<td>Authors</td>
<td>Treatment</td>
<td>Number of Sessions</td>
<td>End Point Measures</td>
<td>Findings and Results</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------------------------</td>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Dover et al&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Multipolar RF + pulsed magnetic fields</td>
<td>6 sessions</td>
<td>marked improvement, 4 = complete clearance Reflectance confocal microscopy Histological analysis (4 patients)</td>
<td>improvement with combined approach of all 3 treatments vs. control areas More reticulated pattern of collagen fibers in combination treated and fractional bipolar RF treated areas Thicker reticular dermis collagen fibers in all treatment areas</td>
</tr>
<tr>
<td>Issa et al&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Ablative fractional RF + Tretinoin cream + acoustic pressure</td>
<td>4 sessions every 4 weeks RF - 45 W Tretinoin - 0.05%</td>
<td>Clinical assessment of severity: 0 = none, 1 = mild, 2 = moderate, 3 = marked, 4 = severe Patient assessment</td>
<td>All patients in combined treatment group showed clinical improvement 4 patients in RF alone group did not show any improvements Erythema, edema and burning sensation in both groups PIH with RF</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment Details</td>
<td>Methods</td>
<td>Score</td>
<td>Outcomes</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------</td>
<td>---------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td>Mishra et al&lt;sup&gt;52&lt;/sup&gt;</td>
<td>Ablative fractional micro-plasma RF</td>
<td>4 sessions every 2 weeks</td>
<td>SR and SA</td>
<td>5</td>
</tr>
<tr>
<td>Shin et al&lt;sup&gt;54&lt;/sup&gt;</td>
<td>Succinylated atelocollagen or placebo vs. succinylated atelocollagen or placebo + ablative fractional CO₂ laser</td>
<td>3 laser sessions performed every 4 weeks CO₂ laser - 50 mJ Abdomen divided into 3 areas</td>
<td>SA</td>
<td>12</td>
</tr>
<tr>
<td>Study</td>
<td>Laser Type</td>
<td>Laser Parameters</td>
<td>Treatment Details</td>
<td>Clinical Outcomes</td>
</tr>
<tr>
<td>-------</td>
<td>------------</td>
<td>-----------------</td>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>de Angelis et al.(^{55})</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1450-nm at 12-55 mJ/mb 2-4 sessions with 4-6 week intervals</td>
<td>SR and SA</td>
<td>51</td>
</tr>
<tr>
<td>Stotland et al.(^{56})</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 12-18 J/cm(^2) 6 sessions with 2-3 week intervals</td>
<td>SR and SA</td>
<td>20</td>
</tr>
<tr>
<td>Bak et al.(^{57})</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 30 mJ 2 sessions with a 4 week interval</td>
<td>SR and SA</td>
<td>22</td>
</tr>
<tr>
<td>Authors</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>Laser Parameters</td>
<td>Number of Sessions</td>
<td>Histological analysis</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Clementoni and Lavagno 
58 | 1565-nm at 50-55 J/cm² 3 sessions with 4-5 week intervals | Not stated                                                                       | 12                 | Increased epidermal and dermal thickness                                                | 51-75% clinical improvement observed in all patients Moderate to good satisfaction recorded by all patients 91.7% and 83.3% showed >50% improvement in volume and color respectively | Erythema Edema Crusting             |
| Wang et al 
59     | Abdomen split into 2 and treated with 1540-nm at 50 J/cm² vs. 1410-nm at 30 J/cm² 6 treatments at 3-6 week intervals | SR and SA                                                                        | 9                  | All patients demonstrated clinical improvement 28% of 1410-nm treated and 33% of 1540-nm treated groups had good or excellent improvements 71.4% and 28.6% of patients were very satisfied and moderately satisfied respectively Increased epidermal thickness, dermal thickness and collagen | Pain and PIH particularly with 1540-nm and 1410-nm lasers respectively Pruritus |
and elastin density vs. baseline with no significant differences between lasers

<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Laser Type</th>
<th>Laser Parameters</th>
<th>Treatment Details</th>
<th>Clinical Improvement</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malekzad et al\textsuperscript{61}</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1540-nm at 50-70 J/cm\textsuperscript{2}</td>
<td>4 sessions at 4 week intervals</td>
<td>SA 9</td>
<td>Clinical improvement: 1 = 0%, 2 = 1-24%, 3 = 25-64%, 4 = 65-94%, 5 = 95-100%</td>
</tr>
<tr>
<td>Kim et al\textsuperscript{18}</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1550-nm at 15 mJ/MTZ</td>
<td>1 session</td>
<td>Normal adjacent skin and untreated striae used as controls</td>
<td>SA 6</td>
</tr>
<tr>
<td>Alves et al\textsuperscript{62}</td>
<td>Fractional non-ablative Er:glass laser</td>
<td>1540-nm at 70 mJ/MTZ</td>
<td>3-6 sessions</td>
<td>SR 4</td>
<td>Clinical appearance</td>
</tr>
</tbody>
</table>

PIH = Postinflammatory Hyperpigmentation
SR = Subjective Response
Guimarães et al\textsuperscript{63} & Fractional non-ablative Er:glass laser & 1550-nm at 80-100 mJ/MTZ 4-8 sessions at 4 week intervals & SR & 10 & Clinical improvement and patient satisfaction score: 0 (no improvement) – 10 (total improvement) & Mean clinical improvement of 8.4 after an average of 6.5 sessions Mean patient satisfaction score of 8.2 & PIH & 4 \\
Katz et al\textsuperscript{64} & Fractional non-ablative Er:glass laser & 1550-nm at 20-70 mJ/MTZ 3-5 sessions at 4 week intervals & SR & 2 & Clinical appearance Patient satisfaction & >75% improvement in both patients Both patients highly satisfied with results & Erythema Edema & 4 \\
Lee et al\textsuperscript{65} & Fractional ablative CO\textsubscript{2} laser & 10,600-nm at 10 mJ/MTZ 1 session Retrospectively reviewed & SA & 27 & Clinical improvement: 0 = worsened, 1 = 0-25%, 2 = 26-50%, 3 = 51-75%, 4 = >75% Patient satisfaction: unsatisfied, slightly satisfied, satisfied, very satisfied & 7.4% had grade 4 improvement, 51.9% had grade 3 improvement, 33.3% had grade 2 improvement and 7.4% had grade 1 improvement 22.2% of patients were very satisfied, 51.9% were satisfied, 18.1% were slightly satisfied, & PIH Pruritus Crusting Oozing Erythema & 4
<table>
<thead>
<tr>
<th>Authors</th>
<th>Treatment 1</th>
<th>Treatment 2</th>
<th>Clinical Improvement</th>
<th>PIH</th>
<th>Pain during Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naeini and Soghrati-66</td>
<td>Fractional ablative CO₂ laser (group 1) vs. GCA + Tretinoin (group 2)</td>
<td>10,600-nm at 16 J/cm² 5 sessions with 2-4 week intervals 10% GCA + 0.05% Tretinoin daily Striae from same individual randomly assigned to different treatment groups</td>
<td>6</td>
<td>Clinical improvement: weak = 0-25%, moderate = 25-50%, good = 50-75%, excellent = &gt;75% Patient satisfaction: 0 (no improvement) to 10 (complete improvement) Surface area of striae</td>
<td>Significantly higher clinical improvements in group 1 (27%) vs. group 2 (5.2%) Mean difference in striae surface area significantly lower in group 1 (-37.1 cm) vs. group 2 (-7.9 cm) Mean patient satisfaction scores significantly higher in group 1 (3.05) vs. group 2 (0.63)</td>
</tr>
<tr>
<td>Yang and Lee-67</td>
<td>Fractional non-ablative Er:glass laser vs. Fractional ablative CO₂ laser</td>
<td>Er:glass laser - 1550-nm at 50 mJ CO₂ laser - 10,600-nm at 40-50 mJ 3 sessions at 4 week intervals Treatments randomized</td>
<td>22</td>
<td>Clinical improvement: 0 = no improvement, 1 = &lt;25%, 2 = 26-50%, 3 = 51-75%, 4 = &gt;76% Patient satisfaction: 0 = not satisfied, 1 = slightly satisfied, 2 = satisfied, 3 = very satisfied, 4 =</td>
<td>Clinical improvements observed in 90.9% of striae in both treatment groups Increased skin elasticity and reduced width of striae with both treatments from baseline 81.8% of patients judged their striae as</td>
</tr>
<tr>
<td>Naeini et al\textsuperscript{68}</td>
<td>Fractional ablative CO\textsubscript{2} laser + fractionated microneedle RF vs. fractionated microneedle RF</td>
<td>CO\textsubscript{2} laser - 10,600-nm at 16 J/cm\textsuperscript{2} Laser + RF - 5 sessions with 4 week intervals RF only – 3 sessions with 4 week intervals Opposite sides of body randomly assigned to each treatment group</td>
<td>SA 6</td>
<td>Clinical improvement: 0-25%, 25-50%, 50-75%, &gt;75% Patient satisfaction: 0 (lack of improvement) to 10 (complete improvement) Surface area of striae</td>
<td>Significantly higher clinical improvement and patient satisfaction scores in CO\textsubscript{2} laser + RF group vs. RF alone Greater reductions in mean surface area of striae with CO\textsubscript{2} laser + RF vs. RF alone</td>
</tr>
<tr>
<td>Authors</td>
<td>Laser Type</td>
<td>Wavelengths/Parameters</td>
<td>Intervals</td>
<td>Clinical Improvement</td>
<td>Histological Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------</td>
<td>------------------------</td>
<td>-----------</td>
<td>----------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Ryu et al.</td>
<td>Fractional ablative CO₂ laser vs. fractionated microneedle RF vs. combination</td>
<td>CO₂ laser – 700 to 1000 mJ RF – 4-7 intensity</td>
<td>3 treatment sessions with 1 month intervals</td>
<td>Not stated</td>
<td>Clinical improvement: 1 = 0-30%, 2 = 30-50%, 3 = 51-80%, 4 = ≥81%</td>
</tr>
<tr>
<td>Gungor et al.</td>
<td>Ablative Er:YAG laser vs. non-ablative Nd:YAG laser</td>
<td>Er:YAG laser - 2940-nm at 3.2 J + 1 J Nd:YAG laser - 1064-nm at 50 J/cm²</td>
<td>3 sessions at monthly intervals</td>
<td>SR and SA</td>
<td>Clinical improvement: &lt;33% = poor, 33-66% = moderate, &gt;66% = good</td>
</tr>
<tr>
<td>Tay et al.</td>
<td>Non-ablative diode laser</td>
<td>1450-nm at 4,8 and 12 J/cm²</td>
<td>3 sessions with 6 week intervals</td>
<td>SR and SA</td>
<td>Clinical improvement: 1 = ≤25%, 2 = 26-50%, 3 = 51-75%, 4 = &gt;75%</td>
</tr>
</tbody>
</table>

**Ryu et al.**

- **Laser Type:** Fractional ablative CO₂ laser vs. fractionated microneedle RF vs. combination
- **Wavelengths/Parameters:** CO₂ laser – 700 to 1000 mJ RF – 4-7 intensity
- **Intervals:** 3 treatment sessions with 1 month intervals
- **Clinical Improvement:** Not stated
- **Histological Description:** Clinical improvement: 1 = 0-30%, 2 = 30-50%, 3 = 51-80%, 4 = ≥81%
- **Notes:** Histological analysis (2 patients)

**Gungor et al.**

- **Laser Type:** Ablative Er:YAG laser vs. non-ablative Nd:YAG laser
- **Wavelengths/Parameters:** Er:YAG laser - 2940-nm at 3.2 J + 1 J Nd:YAG laser - 1064-nm at 50 J/cm²
- **Intervals:** 3 sessions at monthly intervals
- **Clinical Improvement:** SR and SA
- **Histological Description:** Clinical improvement: <33% = poor, 33-66% = moderate, >66% = good
- **Notes:** Histological analysis (6 patients)

**Tay et al.**

- **Laser Type:** Non-ablative diode laser
- **Wavelengths/Parameters:** 1450-nm at 4,8 and 12 J/cm²
- **Intervals:** 3 sessions with 6 week intervals
- **Clinical Improvement:** SR and SA
- **Histological Description:** Clinical improvement: 1 = ≤25%, 2 = 26-50%, 3 = 51-75%, 4 = >75%
- **Notes:** Patient satisfaction: A = not satisfied, B
- **Notes:** No noticeable improvements when compared with control
- **Notes:** Erythema and PIH
<table>
<thead>
<tr>
<th>Study authors</th>
<th>Treatment</th>
<th>Parameters</th>
<th>Control</th>
<th>Clinical improvement</th>
<th>Histological analysis</th>
<th>Side effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hernández-Perez et al(^{72})</td>
<td>IPL</td>
<td>515-1200-nm 5 sessions with 2 week intervals</td>
<td>SA</td>
<td>Clinical improvement: scale by crosses – 0 = no improvement, + = mild, ++ = moderate, +++ = good, ++++ = very good Length and number of striae Histological analysis</td>
<td>Clinical improvement was moderate in 40%, good in 20% and very good in 40% Reduced total length and number of striae Improved collagen fiber quality Increased dermal thickness (2.03 mm pre treatment vs. 3.31 mm post treatment)</td>
<td>PIH</td>
<td>4</td>
</tr>
<tr>
<td>Bedewi and Khalafawy(^{73})</td>
<td>IPL</td>
<td>535, 550 + 580 nm at 25-35 J/cm(^2) 5 sessions with 3-4 week intervals</td>
<td>SR and SA</td>
<td>Synchrotron IR microspectroscopic study of dermal fibroblasts Histological analysis</td>
<td>Increased collagen, amide1 and beta sheet expression following IPL treatment</td>
<td>Stinging sensation</td>
<td>4</td>
</tr>
<tr>
<td>El Taieb and Ibrahim(^{74})</td>
<td>Fractional ablative CO(_2) laser vs. IPL</td>
<td>CO(_2) laser - 10,600-nm at 40 mJ 5 sessions with 1 month intervals IPL - 590-nm at 20-30</td>
<td>Not stated</td>
<td>Clinical improvement: 1 = ≤50%, 2 = &gt;50% Width and length of striae Patient satisfaction: none or less satisfied = 0, 80% and 32% were deemed to have ≥50% improvement in the laser and IPL groups respectively Significant improvements in striae width in both groups but</td>
<td>Erythema Burning Pruritus PIH (Occurrence rates within each treatment group not stated)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Study Authors</td>
<td>Treatment</td>
<td>Energy Density</td>
<td>Session Details</td>
<td>Outcome Measures</td>
<td>Results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------</td>
<td>----------------</td>
<td>------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al-Dhalimi Abo Nasyria\textsuperscript{75}</td>
<td>IPL</td>
<td>650-nm at 13-15.5 J/cm\textsuperscript{2} vs. 590-nm at 13-14.5 J/cm\textsuperscript{2} 5 sessions with 2 week intervals Different wavelengths used on opposite sides of body</td>
<td>SR 20 Sum of length and width of striae Erythema: 0-1 white, &gt;1-4 mild, &gt;4-7 moderate, &gt;7-10 severe Patient satisfaction: weak, partial, very good</td>
<td>Significant reductions in length and width with both treatments Significant reduction in erythema with 590-nm wavelength along with superior patient satisfaction scores Erythema Pain Burning PIH All more common with 590-nm wavelength</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aust et al\textsuperscript{76}</td>
<td>PCT</td>
<td>1 session Not stated</td>
<td>SR and SA 16 Clinical improvement: no change (0%), Marked to excellent improvement in 43.8% with minimal to Pain Erythema Spotty</td>
<td>Improved skin texture, tightening and dermal neovascularization No change in pigmentation Increased collagen I and elastin No change in collagen III</td>
<td>None stated 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park et al\textsuperscript{77}</td>
<td>PCT</td>
<td>3 sessions with 4 week intervals</td>
<td>SR and SA 16 Clinical improvement: no change (0%), Marked to excellent improvement in 43.8% with minimal to Pain Erythema Spotty</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient satisfaction: unsatisfied, somewhat satisfied, highly satisfied</td>
<td>Histological analysis</td>
<td>bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>minimal (&lt;25%), moderate (26-50%), marked (51-75%), excellent (76-100%) Patient satisfaction: unsatisfied, somewhat satisfied, highly satisfied Histological analysis</td>
<td>moderate in the remaining patients 37.5% were highly satisfied, 50% somewhat satisfied, 12.5% unsatisfied Increased dermal elastin and collagen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nassar et al\textsuperscript{78}  
PCT vs. microdermabrasion + sonophoresis  
PCT - 3 sessions with 4 week intervals Microdermabrasion – 10 sessions over 5 months  
SR and SA  
Clinical improvement: no improvement, mild (≤25%), moderate (26-50%), good (51-75%), excellent (≥76%)  
Patient satisfaction: not satisfied, slightly satisfied, satisfied, very satisfied, extremely satisfied Histological analysis  
Clinical improvements in 90% of PCT treated group vs. 50% in microdermabrasion + sonophoresis treated group  
Significantly higher satisfaction scores with PCT  
Epidermal thickness, number of fibroblasts and collagen levels were increased in 90% and 50% of the PCT and microdermabrasion + sonophoresis treated groups respectively  
Erythema PIH (more common in microdermabrasion + sonophoresis group)  

| Khater et al\textsuperscript{79} | PCT vs. fractional ablative CO\textsubscript{2}  
PCT – 3 sessions with 4 week  
SR and SA  
Clinical improvement: none, mild (≤25%),  
Clinical improvements in 90% of PCT treated group vs. 50% in laser  
Erythema PIH (more common in laser group) | 2 |
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Intervals</th>
<th>Intensity</th>
<th>Clinical Improvement</th>
<th>Patient Satisfaction</th>
<th>Histological Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al 80</td>
<td>Intradermal RF + PRP</td>
<td>3 sessions with 4 week intervals</td>
<td>RF - 12 W</td>
<td>Clinical improvement: no change, mild (0-25%), moderate (25-50%), marked (50-75%), excellent (≥76%)</td>
<td>not stated</td>
<td>Patient satisfaction: not satisfied, slightly satisfied, satisfied, very satisfied, extremely satisfied</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>treated group</td>
<td>Significantly higher satisfaction scores with PCT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Epidermal thickness, number of fibroblasts and collagen levels were increased in 90% and 50% of the PCT and laser treated groups respectively</td>
</tr>
<tr>
<td>Suh et al 81</td>
<td>Plasma fractional RF + PRP + US</td>
<td>3 sessions with 3 week intervals</td>
<td>SA</td>
<td>Clinical improvement: no improvement, mild (&lt;25%), moderate (25-49%), good (50-74%), excellent (&gt;75%)</td>
<td>Excellent improvement in 33%, 38.9% very good, 22.4% good, 5.6% mild</td>
<td>Excellent improvement in 33%, 38.9% very good, 22.4% good, 5.6% mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Average reduction in width of striae from 0.75 mm to 0.27 mm</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Sessions &amp; Intervals</td>
<td>Clinical Improvement</td>
<td>Clinical Improvement</td>
<td>Erythema</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>---------------------</td>
<td>----------------------</td>
<td>----------------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Agamia et al.⁸²</td>
<td>PCT vs. PCT + PRP</td>
<td>4 sessions with 2 week intervals PCT alone on right side of body with left side receiving PCT + PRP</td>
<td>Not stated</td>
<td>Clinical improvement: none, minimal, moderate, marked</td>
<td>None stated</td>
<td></td>
</tr>
<tr>
<td>Trelles et al.⁸³</td>
<td>Infrared light</td>
<td>800-1800-nm at 31 J/cm² 4 sessions with 15 day intervals</td>
<td>SA</td>
<td>Clinical improvement: worse, same, fair, good, very good Striae depth</td>
<td>Erythema</td>
<td></td>
</tr>
<tr>
<td>Bitencourt et al. 84</td>
<td>Galvanopuncture</td>
<td>10 sessions once a week at 200 μA</td>
<td>SA</td>
<td>32</td>
<td>Clinical improvement: no improvement, slight (1-25%), moderate (26-50%), good (51-75%), very good (76-100%)</td>
<td>Plasma inflammatory marker levels</td>
</tr>
</tbody>
</table>

### Supplemental Table III: Summary and LOE for treatments used to reduce vascularity in SD.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Wavelength/Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldman et al&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Long-pulsed Nd:YAG laser</td>
<td>1064-nm at 80-100 J/cm&lt;sup&gt;2&lt;/sup&gt; Average number of treatment sessions was 3.45 with 3-6 week intervals</td>
<td>SR</td>
<td>20</td>
<td>Clinical improvement: poor = ≤30%, good = 30-70%, excellent = &gt;70%</td>
<td>Improvement rated as excellent by 55% of patients and 40% of doctors</td>
<td>Edema</td>
<td>4</td>
</tr>
<tr>
<td>Elsaie et al&lt;sup&gt;60&lt;/sup&gt;</td>
<td>Long-pulsed Nd:YAG laser</td>
<td>Striae divided into 3 sections and treated with 1064-nm at 75 J/cm&lt;sup&gt;2&lt;/sup&gt; vs. 100 J/cm&lt;sup&gt;2&lt;/sup&gt; vs. control 4 treatments at 3 week intervals</td>
<td>SR and SA</td>
<td>45</td>
<td>Global Aesthetic improvement scale: 1 (much improved) to 5 (no change) Patient satisfaction: 1 (very satisfied) to 5 (very unsatisfied) Length and width of striae Histological analysis (6 patients)</td>
<td>Clinical improvements in SA and SR with both fluencies Better results in SA observed using 100 J/cm&lt;sup&gt;2&lt;/sup&gt; All patients satisfied with results (no further information given) Significant improvements in length and width of striae in both groups Increased collagen and elastin fibers with both fluencies</td>
<td>Pain, PIH (Occurrence rates for each fluence not stated)</td>
<td>2</td>
</tr>
<tr>
<td>Study</td>
<td>Method</td>
<td>Parameters</td>
<td>Protocol Duration</td>
<td>Analysis</td>
<td>Observations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-------------------</td>
<td>----------</td>
<td>-------------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jiménez et al 85</td>
<td>PDL</td>
<td>585-nm at 3 J/cm² 2 treatments 6 weeks apart Untreated striae acted as controls</td>
<td>20</td>
<td>Striae area and color Histological analysis</td>
<td>No significant differences in striae area in treatment vs. control striae Improvement in color in SR No improvement in SA Increased collagen in treated striae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shokeir et al 86</td>
<td>PDL vs. IPL</td>
<td>PDL - 595-nm at 2.5 J/cm² IPL - 565-nm at 17.5 J/cm² 5 sessions with 4 week intervals Body area split into two with each side receiving one of the treatments</td>
<td>20</td>
<td>Clinical improvement: 0-5 Striae width Skin texture Histological analysis</td>
<td>Striae width decreased and skin texture improved with both treatments SR showed greater clinical improvements vs. SA PDL induced higher levels of collagen I expression Erythema, pain, itching and PIH recorded with both treatments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McDaniel et al 87</td>
<td>PDL</td>
<td>585-nm 4 treatment protocols (spot diameter, fluence): 1 =</td>
<td>39</td>
<td>Percentage return to normal visual skin patterns Skin shadowing using shadow profilometry</td>
<td>Best results observed with 10 mm spot size + 3 J/cm² fluence All protocols reduced skin shadowing Elastin appeared normal Purpura Erythema Hyperpigmentation Hypopigmentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nehal et al.(^88)</td>
<td>PDL</td>
<td>585-nm at 4.25 J/cm(^2)</td>
<td>SA</td>
<td>5</td>
<td>Clinical appearance</td>
<td>Striae texture</td>
<td>Histological analysis</td>
<td>All 5 patients reported mild improvements in appearance</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Gauglitz et al.(^89)</td>
<td>PDL vs. fractional ablative Er:YAG laser</td>
<td>PDL - 585-nm at 7 J/cm(^2) Er:YAG laser – 2940-nm at 72 J/cm(^2)</td>
<td>SR</td>
<td>2</td>
<td>Clinical appearance</td>
<td>Patient satisfaction</td>
<td>Skin texture</td>
<td>Greater improvements with Er:YAG laser reported in first patient</td>
</tr>
</tbody>
</table>
Nouri et al\textsuperscript{90} | PDL vs. short pulsed CO\textsubscript{2} laser | PDL – 585 nm at 3 J/cm\textsuperscript{2} CO\textsubscript{2} laser – 350 mJ and 400 mJ 1 session Striae split into 3 areas and treated with both + control area | Not stated | 4 | Clinical improvement: “did the treated areas look more like normal skin than the untreated control?” | No improvement with either treatment | PIH with both Erythema with CO\textsubscript{2} laser | 2

Longo et al\textsuperscript{91} | Copper bromide laser | 577 nm at 4-8 J/cm\textsuperscript{2} 1-5 sessions with 1 month intervals | Not stated | 15 | Clinical improvement: Poor, less, good, excellent Striae width, depth and color | 5 patients had total disappearance of striae 8 patients had good improvement 2 patients improvements were categorized as less Results maintained at 2 years in 13 patients | Burning Crusting | 4

**Supplemental Table IV**: Summary and LOE for treatments used to increase melanin in SD and various other topicals.

<table>
<thead>
<tr>
<th>Author</th>
<th>Intervention</th>
<th>Dosage/Regimen</th>
<th>Striae type</th>
<th>Sample size</th>
<th>Outcome measures</th>
<th>Results</th>
<th>Side effects</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sadick et al</td>
<td>UVB/UVA1 light therapy</td>
<td>UVB - 296-315 nm + UVA - 360-370 nm at 45-400 mJ/cm² Twice weekly treatments for a maximum of 10 treatments Adjacent area acted as control</td>
<td>SA</td>
<td>9</td>
<td>Repigmentation: 0-25%, 26-50%, 51-75%, 76-100%, &gt;100% Histological analysis (2 patients)</td>
<td>After final treatment 5 patients had &gt;100% pigmented striae (hyperpigmented), 3 had 76-100% and 1 had 51-75% improvement After 12 weeks 2 patients had 51-75% improvement, 3 had 26-50% improvement, and 4 had 0-25% improvement Increase in elastic fiber to collagen ratio in 1 patient</td>
<td>Erythema PIH</td>
<td>2</td>
</tr>
<tr>
<td>Goldberg et al</td>
<td>XeCl excimer laser</td>
<td>308 nm at 150-900 J/cm² Up to 15 sessions</td>
<td>SA</td>
<td>75</td>
<td>Repigmentation: none (0%), mild (1-25%), moderate (26-75%), substantial (76-100%) Patient evaluations: worsened, no change, improved</td>
<td>All subjects achieved ≥76% darkening of their striae 80% noted improvement in appearance of striae Mild to moderate erythema in all patients</td>
<td>Splaying of pigment</td>
<td>4</td>
</tr>
</tbody>
</table>

Click here to download Supplemental Table, for Online-Only Publication (in .doc format ONLY): Supplemental Table IV.docx
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Parameters</th>
<th>Sites</th>
<th>Sessions</th>
<th>Endpoints</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexiad-&lt;br&gt;es-Armenakas et al&lt;sup&gt;94&lt;/sup&gt;</td>
<td>XeCl excimer laser</td>
<td>308 nm at minimal erythema dose minus 50 mJ/cm². Up to 10 sessions with 2 week intervals. Site matched controls used.</td>
<td>SA</td>
<td>9</td>
<td>Repigmentation: 0-100% by visual and colorimetric assessment</td>
<td>Mean pigmentation correction after 9 treatments by visual and colorimetric assessment of 68% and 102% respectively vs. control. Both values declined over 6-months.</td>
</tr>
<tr>
<td>Ostovari et al&lt;sup&gt;95&lt;/sup&gt;</td>
<td>XeCl excimer laser</td>
<td>308 nm. Up to 10 sessions with weekly intervals.</td>
<td>SA</td>
<td>10</td>
<td>Repigmentation and patient satisfaction: poor (0-25%), moderate (26-50%), good (51-75%), very good (76-100%). Colorimetric analysis.</td>
<td>80% of patients had poor or moderate results. 70% of patients rated their results as poor or moderate. Poor effect on repigmentation.</td>
</tr>
<tr>
<td>Goldberg et al&lt;sup&gt;96&lt;/sup&gt;</td>
<td>XeCl excimer laser vs. UVB light</td>
<td>XeCl – 308 nm. UVB – 290-320 nm. Up to 10 treatments.</td>
<td>SA</td>
<td>10 (5 XeCl laser, 5 UVB light)</td>
<td>Histological analysis of melanocytes</td>
<td>Increase in melanin Hypertrophy and increase of melanocytes with both treatments.</td>
</tr>
<tr>
<td>Summe-&lt;br&gt;oil&lt;sup&gt;®&lt;/sup&gt;</td>
<td>Bio-oil&lt;sup&gt;®&lt;/sup&gt;</td>
<td>Twice daily</td>
<td>Not</td>
<td>20</td>
<td></td>
<td>Significant</td>
</tr>
<tr>
<td>Study</td>
<td>Treatment</td>
<td>Duration</td>
<td>Number</td>
<td>Observer Scar Assessment Scale</td>
<td>Clinical Evaluation</td>
<td>Outcomes</td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------------------</td>
<td>----------------------------------</td>
<td>--------</td>
<td>--------------------------------</td>
<td>---------------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>rs et al&lt;sup&gt;100&lt;/sup&gt;</td>
<td>Abdomen split into two with one half acting as a control</td>
<td>stated</td>
<td></td>
<td>5 parameters (vascularization, pigmentation, thickness, relief, pliability) graded 1 (best) to 10 (worst)</td>
<td>Observer Scar Assessment Scale: improvements in treated striae vs. untreated striae</td>
<td></td>
</tr>
<tr>
<td>Buchan-an et al&lt;sup&gt;100&lt;/sup&gt;</td>
<td>Cocoa butter vs. placebo</td>
<td>Daily 12-15 weeks gestation until delivery</td>
<td>Not stated</td>
<td>300 (150 treatment, 150 placebo)</td>
<td>Development of new striae: 0 (no striae) to 4 (severe striae)</td>
<td>No significant differences in the development of new striae between treatment vs. placebo group</td>
</tr>
<tr>
<td>Osman et al&lt;sup&gt;101&lt;/sup&gt;</td>
<td>Cocoa butter vs. placebo</td>
<td>Daily 12-18 weeks gestation until delivery</td>
<td>Not stated</td>
<td>175 (91 treatment, 84 placebo)</td>
<td>Development of new striae and severity: 1 = mild, 2 = moderate, 3 = severe</td>
<td>No significant differences in the development or severity of striae between treatment vs. placebo</td>
</tr>
<tr>
<td>Soltanipoor et al&lt;sup&gt;102&lt;/sup&gt;</td>
<td>Olive oil</td>
<td>Twice daily 18-20 weeks gestation</td>
<td>Not stated</td>
<td>100 (50 treatment, 50 control)</td>
<td>Development of new striae and severity: 0 = none, 1 = few, 2 = numerous</td>
<td>No significant differences in the development or severity of striae between treatment vs. control</td>
</tr>
<tr>
<td>Taavoni et al&lt;sup&gt;103&lt;/sup&gt;</td>
<td>Olive oil</td>
<td>Twice daily 18-20 weeks gestation</td>
<td>Not stated</td>
<td>70 (35 treatment, 35)</td>
<td>Development of new striae</td>
<td>No significant differences in the development of striae</td>
</tr>
</tbody>
</table>

Mild self-limiting allergic reaction

None stated
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Details</th>
<th>Duration</th>
<th>Participants</th>
<th>Outcome Measures</th>
<th>Results</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taşhan and Kafkasli</td>
<td>Almond oil vs. almond oil + massage</td>
<td>8 weeks</td>
<td>141 (48 almond oil, 47 almond oil with massage, 46 control)</td>
<td>Development of new striae</td>
<td>Significant differences observed between all 3 groups Almond oil + massage group developed fewest striae</td>
<td>None stated</td>
</tr>
<tr>
<td></td>
<td>Every other day from 19 to 32 weeks gestation</td>
<td>control</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Daily from 32 weeks gestation until delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not stated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soltanipour et al</td>
<td>Olive oil vs. Saj&lt;sup&gt;®&lt;/sup&gt; cream (lanolin, stearin, triethanolamine, almond oil and bizovax glycerin amidine)</td>
<td>Twice daily from 18-20 weeks until 38-40 weeks gestation Untreated subjects acted as controls</td>
<td>150 (50 olive oil, 50 Saj&lt;sup&gt;®&lt;/sup&gt;, 50 control)</td>
<td>Development of new striae: abdomen divided into 4 quadrants – 0 = no striae, 1 = striae which do not affect a quadrant completely, 2 = striae which affect a quadrant completely 1-3 = mild, 4-6 = moderate, 7-8 = severe</td>
<td>No significant differences in the development or severity of striae between any of the groups</td>
<td>None stated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Ud-din et al</td>
<td>Topical silicone gel vs. placebo</td>
<td>Daily for 6 weeks Placebo applied to opposite side of abdomen</td>
<td>20</td>
<td>Severity, self conscious and impact scores Histological analysis</td>
<td>No significant changes in severity, self conscious or impact scores Decreased hemoglobin and collagen with</td>
<td>None stated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>LOE – level of evidence, SR – striae rubrae, SA – striae albae, XeCl – xenon chloride, PIH – postinflammatory hyperpigmentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>increased melanin in both silicone and placebo treated sides</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collagen levels significantly higher with lower melanin levels in treatment group vs. placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
REQUIRED SUBMISSION FORM AND CHECKLIST FOR AUTHORS

(Photocopy this page, complete all applicable sections, and submit with manuscript)

Corresponding Author: Ardeshir Bayat

Phone No.:+44(0)161 3060607 Fax No.: _______________ E-mail: ardeshr.bayat@manchester.ac.uk

☑ Cover letter:
  - Title, brief description of manuscript and its significance to dermatologists
  - Suggested section
  - Explanation of any conflicts of interest
  - Possible reviewers

☑ Title page (in word document format only)
  - Title of article
  - Full name(s), academic degrees, and academic, institutional, and relevant corporate affiliations of author(s)

☑ All writers and contributors who participated in the preparation of the manuscript are listed as authors, (see Authorship Statement form)

☑ Name, address, business telephone and fax numbers, and E-mail address of author to whom correspondence should be sent.

☑ Statement of all funding sources for the work. If none, please state: This article has no funding source.

☑ Publishable disclosure statement of potential conflicts of interest for each author. If none, please state: The authors have no conflict of interest to declare.

☐ Statement on any prior presentation

☐ Reprint request line

☑ Text word count, number of references, tables, and figures

☑ Manuscript document (in word document format only)
  - Manuscript is double-spaced with each section beginning on a new page
  - Number the pages in the upper-right corner
  - Abstract (structured, if required) begins the manuscript submission
  - Submission has continuous line-numbering
  - Abbreviation and acronym list, starting on a separate page
  - References (double-spaced), starting on a separate page
  - Figure legend (double-spaced), starting on a separate page

☑ Tables, each uploaded as a separate file (in word document format only)

☑ Figures, each uploaded as a separate file (in .jpg, .tif, or .eps format only) and are a minimum of 300 dpi

☑ Signed Copyright Transfer Statement with signature from each author (online submission only)

☑ Signed from each author (online submission only)

☑ Signed Conflict of Interest Statement from each author (online submission only)

☐ All human and animal studies are approved by an Institutional Review Board
  - Copy of Institutional Review Board approval for clinical research trials (online submission only)

☐ CONSORT checklist for randomized trials (online submission only)

☐ Patient consent letters (photographic and informed consent, online submission only)

☐ Permission to reproduce material published previously (online submission only)

☑ Contents of the manuscript have not been previously published and are not currently submitted elsewhere

☑ I accept responsibility for the scientific integrity of the work described in this manuscript

☑ All listed authors have seen and approved of the manuscript and will sign off on any subsequent manuscript revisions

[Signature]

Signature of corresponding author who verifies that above is correct __________________ Date __________________

*Manuscript Checklist
*Click here to download Manuscript Checklist: JAAD_Submission_Checklist.pdf
AUTHORSHIP DECLARATION

Each author must fill out a separate copy of this form.

All persons and only persons who meet authorship criteria should be listed as authors. Criteria for authorship include having performed at least one of the tasks listed in boxes #1-6 below and having read and approved the final version of the paper. All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, and/or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Journal of the American Academy of Dermatology. If this study has been or will be presented at a national meeting, indicate the appropriate information on the title page.

Acknowledgment: All persons who have made substantial contributions to the work reported in the manuscript, including but not limited to generating data, performing statistical analysis, and/or substantial editing that affects the content of the paper, but whose contribution is not sufficient to warrant inclusion as an author, should be listed in the Acknowledgment along with their affiliation(s) and funding source(s), if any, and have given the Journal permission to be named. If I (we) do not include an acknowledgment, that means I (we) have not received substantial contributions from nonauthors.

The author’s name must be typed or clearly printed beneath the signature. Each author must indicate which of the following aspects of the work he or she participated in by checking the box(es) that apply. (It is not necessary for each author to check each of the boxes.) At least one of boxes 1-6 below must be applicable and checked by each author. Box number 9 must also be applicable to each author and must be checked.

☐ 1. I participated in designing the study.
☐ 2. I participated in generating the data for the study.
☐ 3. I participated in gathering the data for the study.
☐ 4. I participated in the analysis of the data.
☐ 5. I wrote the majority of the original draft of the paper.
☐ 6. I participated in writing the paper.
☐ 7. I have had access to all of the raw data of the study.
☐ 8. I have reviewed the pertinent raw data on which the results and conclusions of this study are based. MANDATORY FOR FIRST OR SENIOR AUTHOR.
☐ 9. I have approved the final version of this paper. MANDATORY FOR EACH AUTHOR.
☐ 10. I guarantee that all individuals who meet the Journal’s authorship criteria are included as authors of this paper. MANDATORY FOR CORRESPONDING AUTHOR.
☐ 11. The name(s) and affiliation(s) of the individual(s) who performed the statistical analyses of this work are listed here. (To be filled in by corresponding author.)

________________________________________________________

________________________________________________________

Author(s) signature(s)                                                                 Date signed

________________________________________________________

Signature

Adam Hague

Name (typed or printed)
AUTHORSHIP DECLARATION

Each author must fill out a separate copy of this form.

All persons and only persons who meet authorship criteria should be listed as authors. Criteria for authorship include having performed at least one of the tasks listed in boxes #1-6 below and having read and approved the final version of the paper. All authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, and/or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Journal of the American Academy of Dermatology. If this study has been or will be presented at a national meeting, indicate the appropriate information on the title page.

Acknowledgment: All persons who have made substantial contributions to the work reported in the manuscript, including but not limited to generating data, performing statistical analysis, and/or substantial editing that affects the content of the paper, but whose contribution is not sufficient to warrant inclusion as an author, should be listed in the Acknowledgment along with their affiliation(s) and funding source(s), if any, and have given the Journal permission to be named. If I (we) do not include an acknowledgment, that means I (we) have not received substantial contributions from nonauthors.

The author’s name must be typed or clearly printed beneath the signature. Each author must indicate which of the following aspects of the work he or she participated in by checking the box(es) that apply. (It is not necessary for each author to check each of the boxes.) At least one of boxes 1-6 below must be applicable and checked by each author. Box number 9 must also be applicable to each author and must be checked.

☐ 1. I participated in designing the study.
☐ 2. I participated in generating the data for the study.
☐ 3. I participated in gathering the data for the study.
☐ 4. I participated in the analysis of the data.
☐ 5. I wrote the majority of the original draft of the paper.
☐ 6. I participated in writing the paper.
☐ 7. I have had access to all of the raw data of the study.
☐ 8. I have reviewed the pertinent raw data on which the results and conclusions of this study are based. MANDATORY FOR FIRST OR SENIOR AUTHOR.
☐ 9. I have approved the final version of this paper. MANDATORY FOR EACH AUTHOR.
☐ 10. I guarantee that all individuals who meet the Journal’s authorship criteria are included as authors of this paper. MANDATORY FOR CORRESPONDING AUTHOR.
☐ 11. The name(s) and affiliation(s) of the individual(s) who performed the statistical analyses of this work are listed here. (To be filled in by corresponding author.)

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Author(s) signature(s) Date signed

Signature

Ardeshir Bayat

Name (typed or printed)
Journal of the American Academy of Dermatology
Disclosure Statement of Potential Conflict of Interest

I, Ardeish Bayat, attest that I have submitted for consideration for possible publication in the Journal of the American Academy of Dermatology (JAAD) a manuscript entitled:
Therapeutic targets in the management of striae distensae: A systematic review

I hereby certify that, to the best of my knowledge, (1) the work that is reported on in said manuscript has not received financial support from any pharmaceutical company or other commercial interest except as described below, and (2) neither I nor any first-degree relative has any special financial interest in the subject matter discussed in said manuscript, except as described below. (I understand that an example of one type of such special financial interest would be ownership, by me or a first-degree relative, of a company that sells a product relating to the subject matter of the manuscript.)

Describe any exceptions. Use additional page(s) if space below is insufficient.

1 Commercial Interest: A commercial interest, as defined by the ACCME, is any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients. The ACCME does not consider providers of clinical service directly to patients to be commercial interests. A commercial interest is not eligible for ACCME accreditation.

2 A first-degree relative is defined as a spouse, parents, brothers, sisters, or children of the member.
Disclosure Steps:

A. List the names of commercial interest producing health care goods or services with the exception of non-profit or government organizations and non-health care related companies with which you or your spouse/partner have a financial relationship.

B. Identify the type of ownership interest or compensation you or your first-degree relative² received (ex: salary, honorarium, etc.). The Academy does not need to know the dollar amount.

C. Identify the role you or your first-degree relative have with the commercial interest.

D. If you or your first-degree relative have received multiple items from the same commercial interest or if you or your first-degree relative have had more than one role for the same commercial interest, enter a separate record for each role/item received.

If you have NO financial relationship(s) to disclose:

□ Neither I, the undersigned, nor a first-degree relative, has financial interests/arrangements, affiliations, or other relationships with the commercial supporter(s) of this activity or with any other organization(s) that provide(s) products or services that are relevant to the content for which I am responsible.

If you DO have financial relationship(s) to disclose:

□ I, the undersigned, and/or my first-degree relative currently has a financial interest/arrangement, affiliations, or other relationships with the commercial supporter(s) of this activity or with another organization(s) that provide(s) products or services that are relevant to the content for which I am responsible.

NATURE OF FINANCIAL COMPENSATION

1 Select from the following the role for which you received financial compensation from a commercial interest:

☐ Advisory Board
☐ Board of Directors
☐ Consultant
☐ Employee
☐ Founder
☐ Independent Contractor
☐ Principal Investigator
☐ Speaker
☐ Speaker/Faculty education
☐ Stockholder
☐ Other: please specify:_____________________

² A first-degree relative is defined as a spouse, parents, brothers, sisters, or children of the member.

JAAD Disclosure Statement of Potential Conflict of Interest
2. Select the type of compensation received:

- □ Equipment
- □ Fees
- □ Grants/Research Funding
- □ Honoraria
- □ Non-accredited CME Educational Grant
- □ Patent royalties or other compensation for Intellectual Property Rights
- □ Residency/Fellowship Program Funding
- □ Salary
- □ Stock
- □ Stock Option
- □ No Compensation Received
- □ Other Financial Benefit: please specify: ____________________

I agree to update this form within 30 days after I establish any new financial relationships that could represent potential conflicts of interest.

<table>
<thead>
<tr>
<th>Company Name</th>
<th>For What Role?</th>
<th>What was received?</th>
<th>Money paid to you?</th>
<th>Money paid to your institution?</th>
<th>Purchased with your own funds</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXAMPLE:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC Pharma</td>
<td>Advisory Board</td>
<td>Honoraria</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I agree to update this form within 30 days after I establish any new financial relationships that could represent potential conflicts of interest.

3 This means compensation that your institution received for your efforts on this study.

JAAD Disclosure Statement of Potential Conflict of Interest
Under Commercial Interest Relationships, did you list a relationship as “Other” under the “For What Role” column or “Other Financial Benefit” under “Compensation”? If yes, please describe the relationship. Please also provide additional details about any relationship documented above or that does not meet the designated categories that requires disclosure under the AAD’s Administrative Regulations or merits further explanation.

I hereby grant permission for any such information, or an appropriate summary thereof, to be published in JAAD with the manuscript if the manuscript is accepted for publication.

Signature                                  Date

Ardeshir Bayat
Printed Name
Disclosure Statement of Potential Conflict of Interest

I, __________________________________________, attest that I have submitted for consideration for possible publication in the Journal of the American Academy of Dermatology (JAAD) a manuscript entitled: 

Therapeutic targets in the management of striae distensae: A systematic review

I hereby certify that, to the best of my knowledge, (1) the work that is reported on in said manuscript has not received financial support from any pharmaceutical company or other commercial interest except as described below, and (2) neither I nor any first-degree relative has any special financial interest in the subject matter discussed in said manuscript, except as described below. (I understand that an example of one type of such special financial interest would be ownership, by me or a first-degree relative, of a company that sells a product relating to the subject matter of the manuscript.)

Describe any exceptions. Use additional page(s) if space below is insufficient.

1 Commercial Interest: A commercial interest, as defined by the ACCME, is any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients. The ACCME does not consider providers of clinical service directly to patients to be commercial interests. A commercial interest is not eligible for ACCME accreditation.

2 A first-degree relative is defined as a spouse, parents, brothers, sisters, or children of the member.
Disclosure Steps:

A. List the names of commercial interest producing health care goods or services with the exception of non-profit or government organizations and non-health care related companies with which you or your spouse/partner have a financial relationship.

B. Identify the type of ownership interest or compensation you or your first-degree relative received (ex: salary, honorarium, etc.). The Academy does not need to know the dollar amount.

C. Identify the role you or your first-degree relative have with the commercial interest.

D. If you or your first-degree relative have received multiple items from the same commercial interest or if you or your first-degree relative have had more than one role for the same commercial interest, enter a separate record for each role/item received.

If you have NO financial relationship(s) to disclose:

☐ Neither I, the undersigned, nor a first-degree relative, has financial interests/arrangements, affiliations, or other relationships with the commercial supporter(s) of this activity or with any other organization(s) that provide(s) products or services that are relevant to the content for which I am responsible.

If you DO have financial relationship(s) to disclose:

☐ I, the undersigned, and/or my first-degree relative currently has a financial interest/arrangement, affiliations, or other relationships with the commercial supporter(s) of this activity or with another organization(s) that provide(s) products or services that are relevant to the content for which I am responsible.

NATURE OF FINANCIAL COMPENSATION

1 Select from the following the role for which you received financial compensation from a commercial interest:

☐ Advisory Board
☐ Board of Directors
☐ Consultant
☐ Employee
☐ Founder
☐ Independent Contractor
☐ Principal Investigator
☐ Speaker
☐ Speaker/Faculty education
☐ Stockholder
☐ Other: please specify: _____________________

---

2 A first-degree relative is defined as a spouse, parents, brothers, sisters, or children of the member.

JAAD Disclosure Statement of Potential Conflict of Interest
2. Select the type of compensation received:

- Equipment
- Fees
- Grants/Research Funding
- Honoraria
- Non-accredited CME Educational Grant
- Patent royalties or other compensation for Intellectual Property Rights
- Residency/Fellowship Program Funding
- Salary
- Stock
- Stock Option
- No Compensation Received
- Other Financial Benefit: please specify: ____________________

I agree to update this form within 30 days after I establish any new financial relationships that could represent potential conflicts of interest.

<table>
<thead>
<tr>
<th>Company Name</th>
<th>For What Role?</th>
<th>What was received?</th>
<th>Money paid to you?</th>
<th>Money paid to your institution?(^3)</th>
<th>Purchased with your own funds</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXAMPLE:</td>
<td>Advisory Board</td>
<td>Honoraria</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC Pharma</td>
<td>Member</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I agree to update this form within 30 days after I establish any new financial relationships that could represent potential conflicts of interest.

\(^3\) This means compensation that your institution received for your efforts on this study.
Under Commercial Interest Relationships, did you list a relationship as “Other” under the “For What Role” column or “Other Financial Benefit” under “Compensation”? If yes, please describe the relationship. Please also provide additional details about any relationship documented above or that does not meet the designated categories that requires disclosure under the AAD’s Administrative Regulations or merits further explanation.

I hereby grant permission for any such information, or an appropriate summary thereof, to be published in JAAD with the manuscript if the manuscript is accepted for publication.

Signature

Date

Printed Name
TRANSFER OF COPYRIGHT

I (we), the undersigned author(s), transfer all copyright ownership of the manuscript referenced above to the American Academy of Dermatology, in the event the work is published. I (we) warrant that the article is original, does not infringe upon any copyright or other proprietary right of any third party, is not under consideration by another journal, and has not been published previously. I (we) have reviewed and approve the submitted version of the manuscript and agree to its publication in the *Journal of the American Academy of Dermatology*.

Each author’s name must be written in clear, capital letters beside the signature.

<table>
<thead>
<tr>
<th>Author(s) signature(s)</th>
<th>Date signed</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAM HAGUE</td>
<td></td>
</tr>
<tr>
<td>ARDESHIR BAYAT</td>
<td></td>
</tr>
</tbody>
</table>

US Federal Employees: If you are an employee of the US federal government, please sign the following statement: I was an employee of the US federal government when this work was conducted and prepared for publication; therefore the work lies within the public domain and is not subject to the Copyright Act. Ownership of copyright cannot be transferred. **If you are not a government employee, do not sign here.**

Each author’s name must be written in clear, capital letters beside the signature.

<table>
<thead>
<tr>
<th>Author(s) signature(s)</th>
<th>Date signed</th>
</tr>
</thead>
</table>

**Funding agency requirements and other policies**

I have also been made aware of the journal’s policies with respect to funding agency requirements such as the NIH Public Access policy, and the rapid publication “Articles In Press” service. See Elsevier.com for details.

**FUNDING**

☐ The underlying research reported in the article was funded by the US National Institutes of Health.
☐ The underlying research reported in the article was performed by a Howard Hughes Medical Institute investigator.