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# Radiofrequency therapy and non-cosmetic cutaneous conditions

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#### **Abstract**

**Background:** The need for non-invasive methods in treatment of cutaneous disease has continued to evolve exponentially. Amidst the search for technologies, radiofrequency (RF) has proven efficacious in numerous skin disease processes. Though RF is well known for its cosmetic utility, its mechanism is valued in the treatment of many non-cosmetic cutaneous conditions of various etiologies.

**Objective:** To identify and describe studies in which RF was used to treat non-cosmetic skin conditions and to explore the potential of this modality for further application in dermatologic diseases.

**Methods & Materials:** The PubMed database was utilized to find relevant articles.

**Results:** This search strategy yielded 53 articles that met the eligibility criteria. Non-cosmetic indications discussed in these articles include varicose veins (n=10,550), lymphangioma circumscriptum (n=72), cutaneous neoplasms (n=42), cutaneous leishmaniasis (n=743), acne and acne scarring (n=158), non-acne scarring (n=43), primary axillary hyperhidrosis (n=76), and acute and chronic wounds (n=94).

**Conclusion:** Treatment with RF is an effective, generally non-invasive modality with a relatively short post-procedure recovery time and little potential for severe adverse effects in the treatment of several cutaneous conditions. Further clinical studies would prove useful to assess the efficacy and cost-effectiveness of this treatment.

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Disclosure

#### Introduction

Radiofrequency (RF) is a relatively non-invasive method of targeted tissue destruction and rejuvenation that was introduced to the field of dermatologic electrosurgery in 1950. Since then it has continued to set the standard for tissue remodeling with minimal damage to surrounding healthy tissue.

The technology delivers an electrical energy derived from collisions of charged molecules that heat water in-situ. As the heat travels to predetermined tissue depths it meets resistance at all levels, particularly in adipose tissue. As heat resistance builds thermal cellular damage is sustained. An interplay of inherent electrical tissue properties, penetration depth, and frequency are individualized to match each patients' needs. The resultant cellular damage initiates neocollagenesis and remodeling of existing collagen and elastin in a discretely demarcated zone of tissue necrosis. <sup>2,3</sup> Heated fibroblasts upregulate cytokines, heat shock proteins, and growth factors to promote collagen formation and targeted transient inflammation that remodels collagen and elastin with the deposition of *de novo* hyaluronic acid. This remodeling results in a thickened subcutaneous tissue layer while avoiding necrosis, fibrosis, and damage to vasculature and adnexal structures. <sup>4</sup> Over the course of weeks to months, these changes provide both cosmetic and clinically desired tissue remodeling. <sup>5,6</sup>

The device technology contains both cutting and coagulation abilities and is approved for percutaneous, laparoscopic, and intraoperative coagulation and ablation of soft tissue.<sup>3</sup> Although all RF technologies rely on the same fundamental principles of intra-tissue heating, three main types, monopolar, bipolar and unipolar, allow for flexible application. Monopolar RF requires a grounding electrode in contact with the patient's skin, bipolar RF channels energy between a positive and a negative pole usually housed within the same probe, while unipolar RF uses only one electrode.<sup>1,3</sup> Monopolar RF provides the deepest penetration potential (up to 20mm); however bipolar RF, usually reaching 1–4 mm depending on the distance between electrodes, can be easily combined with other device technologies. Combination devices commonly include fractionation, a diode laser, or multiple sets of electrodes that reach varying depths simultaneously, to match the efficacy of monopolar RF. Unipolar RF's utility lies in its ability to reach large areas of subcutaneous tissue typically15–20mm below the skin surface.<sup>1</sup>

Another differentiation of RF treatments is whether it is continuous or pulsed. Continuous RF is delivered with probe temperatures in an uninterrupted fashion to achieve target tissue destruction. Whereas pulse RF delivers current in 20 ms bursts to keep tissues below 42°C. Neurophysiologic studies show that pulsed RF can relieve pain by altering the transmission of neuronal electrical pain signals without heat-induced tissue destruction. As a result, pulsed RF has become a preferred therapeutic option used for several chronic pain conditions, such as cervical radiculopathy.<sup>7</sup>

The purpose of this review is to identify and describe studies in which RF is used to treat non-cosmetic skin conditions and to explore the potential of this modality for further application in dermatologic diseases. The authors have defined non-cosmetic dermatologic

conditions as clinically apparent primary or secondary cutaneous abnormalities that are either presently symptomatic or have the potential to be symptomatic. Treatment of the sequalae of such conditions is also considered non-cosmetic as the purpose of treatment is to return to the pre-disease, or pre-injury, state of the skin. To that effect, Food and Drug Administration (FDA) approved non-cosmetic dermatologic indications include cutaneous leishmaniasis, acne, acne scarring, varicose veins, non-acne scarring, primary axillary hyperhidrosis, benign cutaneous neoplasms, lymphangioma circumscriptum (LC), and wound healing. Indications that have been excluded on a cosmetic basis are cellulite, skin laxity, wrinkles, rosacea, pigmented lesions, and telangiectasias as these types of effected skin occur over time with natural exposures rather than finite periods of endogenous or exogenous injury.

#### **Methods**

A systematic review was conducted following the PRISMA guidelines. A search for peer reviewed articles was performed in August 2018 on the PubMed database using search terms "radiofrequency ablation" or "radio-frequency" or "RF" and "skin" or "dermatology" entered in sperate pairs. The resulting documents were screened for eligibility based on title, abstract, and full-text as necessary. Review of relevant article bibliographies was also conducted. Articles that examined human subjects, reported clinical outcomes of RF use for skin conditions, and were written in English language were included. Articles that justified their research on cosmetic basis alone, did not report clinical outcomes of RF treatment, reported on animal studies, or were written in languages other than English were excluded.

#### Results

A total of 571 articles published from 1971 until present were retrieved using the search methods described above. A title and abstract screen resulted in 71 articles, with a subsequent full text screen resulting in 53 articles that met the eligibility criteria. These search results are illustrated in the PRISMA diagram in Figure 1.

Reviewed studies consist primarily of case series and reports, but also include randomized control trials (RCT) and non-randomized prospective trials. Total number of reports and subjects involved in relevant indications are as follows: four reports on RF use in acne and acne scarring (n=158), four reports on axillary hyperhidrosis (n=76), 13 reports on varicose veins (n=10,550), four reports on wound healing (n=94), five reports on benign neoplasms or cutaneous lesions (n=42), 10 reports of lymphangioma circumscriptum (n=72), five reports on cutaneous leishmaniasis (n=743), and six reports on non-acne scars (n=43). Study design, levels of evidence, and outcome data were extracted for each article and are summarized in Tables 1–8, while significant findings from indication category are summarized below.

#### Acne vulgaris and acne scarring

Of the four studies that reported the use of RF as treatment of acne, two studied active acne vulgaris, one studied acne scarring alone, and one studied acne and resultant scarring simultaneously. These reports include two head-to-head split-face clinical trials, comparing RF treatment to fractional carbon dioxide laser therapy<sup>8</sup> and fractional microneedling RF.<sup>9</sup>

Patients received a range of 2–4 four treatment sessions. Varying outcome assessments consisted of acne lesion count, sebum production, pore size, acne scar severity, and patient satisfaction.

RF treatment led to moderate improvements in all acne scarring with superior results in rolling scars compared to boxcar or ice-pick scars. Statistically significant improvements were also noted with decreased pore size, lesion counts, and sebum production. <sup>8,9</sup> The majority of subjects (65–100%) expressed satisfaction with treatment tolerability and outcomes and up to 95% reported subjective improvement in their acne. <sup>8–11</sup> The split-face study results favored fractional microneedling RF over fractional carbon dioxide laser and bipolar RF for lesion amount, scar size, and sebum reduction. <sup>8</sup> Adverse events included minor and self-resolving edema, erythema, scabbing, and hyperpigmentation. Further detail of these findings can be found in Table 1.

#### **Primary Axillary Hyperhidrosis**

The four reports on the use of RF for hyperhidrosis include case series, a case report, and a non-randomized control study. Patients received a range of 1–4 treatment sessions with follow up every four weeks for six months. Outcome measures included the hyperhidrosis disease severity index (HDSS), visual analogue score (VAS), dermatology quality of life index (DLQI), starch-iodine sweat testing, transepidermal water loss, sweat gland density, and patient satisfaction. 12–15

Radiofrequency improved axillary hyperhidrosis symptoms in most studied patients, with as high as 95% experiencing decreased size of affected area on the starch-iodine test, <sup>12</sup> an average of HDSS score decrease from 3.4 to 2.1 in 2–5 months, DLQI improvement, and significant VAS decrease from 9 to 4 at five months post-treatment. <sup>12,14</sup> Histological evaluation revealed atrophy and necrosis immediately post-treatment and a decrease in total sweat glands one month post-treatment. <sup>12</sup> Patients satisfaction ranged from 50–90%. Reported adverse events included tingling, erythema, hyperpigmentation, swelling, erosions, compensatory hyperhidrosis and numbness; all of which resolved within six-months. <sup>12,13</sup> These findings are detailed in Table 2.

#### **Wound Healing**

Four studies describing the efficacy of RF in wound healing show the most potential for RF as an adjunct therapy (Table 3). The various cases demonstrate the utility of treatment with pulsed RF energy (Provant<sup>®</sup> Regenesis, Scottsdale, AZ) in combination with negative pressure devices, lower limb off-loading, or dermal replacement therapy.<sup>5,16–18</sup> These regimens achieved healing in 24 weeks for chronic or surgical diabetic wounds, as well as for venous insufficiency ulcers. Pulsed RF treatments were most effective when applied for 30 seconds twice daily for four weeks or until wounds are healed. All wounds decreased in size at varying rates, one reporting 0.13 cm<sup>2</sup> per day.<sup>16</sup> Pulsed RF was also shown to reduce chronic wound pain or exacerbated pain with application of compressive therapy.<sup>5,7</sup> With decreased pain, patients were able to tolerate other necessary treatments, such as debriding, bandage changing, and compressive wraps.<sup>5</sup>

#### **Cutaneous neoplasms**

RF has also proven to be an effective modality for removal of multiple cutaneous neoplasms in disease processes such as neurofibromatosis (Table 4). Reports of patients with Brooke-Spiegler Syndrome, neurofibromatosis I, tuberous sclerosis, and a host of other more common growths, such as seborrheic keratosis, demonstrate a wide application of RF treatment. 6,19–23 The primary outcome measures in these studies were decreased lesion numbers, size, and patient satisfaction. All patients received one treatment session only, except a patient with Brooke-Spiegler Syndrome who received 15 treatment sessions and achieved 100% resolution of his cylindromas and 70% resolution of his trichoepitheliomas. RF was also successfully used in conjunction with dermabrasion for resection of tuberous sclerosis related angiofibromas in a 30-year-old female. This subject had satisfactory results without scarring or depigmentation. 6

RF was shown to be a superior method to surgical excision for cutaneous neurofibromas in 16 neurofibromatosis type I patients as it led to less bleeding and fewer postoperative complications. Except for minimal scarring, all subjects were satisfied with the treatment outcomes. One case report demonstrated how RF treatment made surgical removal of a 20cm wide dermatofibroma protuberans possible by reducing its size to 50% pre-operatively. Twenty-one additional subjects were treated with RF energy for a variety of telangiectasia, cherry and spider angiomas, acrochordons, seborrheic keratosis, dermatofibrosarcoma protuberans, and milium. Among these subjects 78% of vascular and 93% of non-vascular lesions had "excellent" or "good" decrease in lesion size as well as 94% and 84% patient satisfaction, respectively. The only adverse events reported were pain ratings of 3–4 during the procedure.

#### Lymphangioma circumscriptum

Ten case series and reports describe the experiences of 72 patients with symptomatic microcytic lymphatic malformation in various cutaneous and oral locations, including the tongue (Table 5). Patients received 1–8 treatments to achieve outcome objectives, which included smaller lesion size, decreased frequency of symptoms, such as bleeding, and infection, as well as lower recurrence rates. All cases reported over 50% and as high as 88% reduction in lesion size with comparable efficacy in cutaneous and mucosal lesions. <sup>24–33</sup> Patient satisfaction was high, but appeared to wane with longer follow up of five years, with recurrence of lesions being up to 66% in one study. <sup>24</sup> Adverse events included swelling, hypopigmentation, scarring, and intermittent bleeding or infection in the cases of oral LC.

#### **Cutaneous Leishmaniasis**

Radiofrequency therapy was reported in four RCTs and one case series for the treatment of cutaneous leishmaniasis (Table 6). Subjects received 1–4 treatment sessions and were followed for up to a year post-procedure. Outcome measures included infection resolution, or cure rate, recurrence, and patient satisfaction. Various control groups received a variety of treatments including antimony, placebo,<sup>34</sup> intralesional or intramuscular sodium stibogluconate (SSG),<sup>35,36</sup> and intralesional meglumine antimoniate.<sup>37</sup> Complete clinical response was achieved in 69.4–98% of the subjects treated with RF.<sup>34–36,38</sup> RF was shown to be non-inferior to antimony as 73% of both groups achieved complete clinical response,

however, those treated with RF experienced less relapse (6.3% compared to 12.5% of antimony patients). RF was also shown to be comparable to intralesional SSG treatment in 359 subjects who experienced an 83% average cure rate. Adverse events included secondary infections, keloid formation, and local cellulitis.

#### Non-acne scarring

RF treatment for hypertrophic non-acne and burn scars in 43 patients are discussed in one prospective study, three case series, and two case reports (Table 7). Two of the studies utilized RF in combination with acoustic pressure ultrasound to deliver either triamcinolone for hypertrophic scar or retinoic acid for atrophic scars.<sup>39,40</sup> Another case series reported use of non-insulated microneedle fractional RF.<sup>41</sup> Outcome measures included scar size and histologic psuedonodule density. Subjects received 1–4 treatment sessions every 3–4 weeks.

All subjects showed scar improvement. The most significant results included hypertrophic scar size reduction from 4.2 to 2.55cm<sup>2</sup> width and decreased attenuation by 67%.<sup>40</sup> On post-treatment histology atrophic scars showed increased collagen density and hypertrophic scars showed resolution of pseudonodules. Average patient satisfaction was 68%. Adverse events included burning sensation during the procedure, mild erythema, edema, fine scale, and mild atrophy.<sup>39–44</sup>

#### Incompetent great saphenous vein

The most studied indication for RF is treatment of incompetent great saphenous veins, leading to lower leg varicosities. A summary of the findings from fourteen articles about non-cosmetic varicosity treatment with RF can be found in Table 8.<sup>45–58</sup> The treatments used include endovenous thermal ablation (ETA)<sup>45,49,51,52,55</sup> and segmental thermal ablation (STA).<sup>50,57,58</sup> Subjects all received one treatment session per limb and were followed for up to five years post-procedure. Outcome measures include distal venous filling on duplex ultrasound and recanalization.

Duplex ultrasound guided evaluation shows that 94.4% of RF treated limbs remain completely occluded at 36 months post-procedure. One study demonstrated 91.9% occlusion at up to five years post procedure. A retrospective study comparing RF to 1,320 ND:YAG and 810 diode laser treatments showed that ND:YAG had significantly higher rates of occlusion at 5 years post-treatment compared to RF or diode. The highest recanalization rates were 12%. Adverse events included transient erythema, endovenous heat induced thrombus, hyperpigmentation, paresthesia, nonocclusive thrombus, worsening leg swelling, superficial thrombophlebitis, ecchymosis, hematoma, and infection.

#### **Discussion**

The purpose of this review was to describe findings of RF treatment in non-cosmetic dermatologic indications. RF treatment of acne and resultant acne scarring, primary axillary hyperhidrosis, acute and chronic wounds, cutaneous lesions such as neurofibromas, lymphangioma circumscriptum, cutaneous leishmaniasis, hypertrophic non-acne scarring, and varicose veins were included for review. RF literature demonstrates that this modality

has been shown to successfully decrease size, expedite healing, or eliminate disease-associated symptoms in all of the above conditions.

RF has potential to treat recalcitrant moderate to severe acne cystica and associated scarring simultaneously to benefit patients suffering from facial pain, lesion drainage, and protracted self-esteem. The ability of radiofrequency to treat inflammatory conditions such as cystic acne is likely multifactorial. Histopathologic analysis of pre- and post- lesions shows decreased follicular density as well as decreased perifollicular lymphocytic infiltrate and sebaceous gland number. <sup>10</sup> Some results also show thickened and compacted collagen type I and III fibers in the upper and lower layers of the dermis post treatment, <sup>59</sup> while others demonstrate decreased expression of transforming growth factor beta, interleukin 8, and NF kappa B. <sup>9</sup>

RF aids in reduction of primary axillary hyperhidrosis symptoms via destruction of sweat glands. Evidence shows RF superiority compared to treatment mainstays that range from topical aluminum salts to axillary curettage, which may carry risks of scarring and only temporary improvement. <sup>12</sup>

RF treatment of neoplastic conditions, such as cutaneous neurofibromas, LC, and hypertrophic scars is largely successful due to directly targeted dermal depth heating, potentiating both superficial and root cause treatment. RF has shown to be a safe and economical pre-treatment for lesion size reduction, adjunct therapy to deliver medication more precisely, or an alternative to traditional surgical approaches as it is minimally invasive, decreases blood loss, and minimizes scarring.

A similar method of microtissue destruction via collagen contraction is fundamental to RF treatment of incompetent veins. RF generated heat causes segmental venous spasms and collagen shrinkage with minimal thrombus formation. <sup>52</sup> Evidence for this therapy shows that RF is comparable to surgical interventions in efficacy, but superior in reducing surgical risk factors, such as infection, post-operative pain, and bruising. Though RF is a well-studied minimally invasive alternative to surgery, head-to-head comparison with 1,320nm ND:YAG shows shortcomings in complete occlusion associated with RF at 5 years post-treatment. <sup>56</sup> Future studies may show that laser ablative modalities may have superior long term efficacy compared to RF.

RF was also shown to successfully treat cutaneous leishmaniasis, in which one week of daily RF thermotherapy is lethal to the assaulting parasite (maximum heat tolerance of 39°C). This offers an alternative to lengthy courses of SSG inoculations and potentially higher patient treatment compliance.<sup>35</sup> Unfortunately, access to electricity and technology support in resource poor regions with endemic cutaneous leishmaniasis is a significant practical limitation.

A limitation of this review is that the majority of reports are case series. In addition, only a small number of studies are available for some of the discussed indications, such as wound healing and cutaneous leishmaniasis. Furthermore, because RF is a novel therapeutic modality, our analysis of the current literature shows that there is a lack of uniform treatment guidelines or protocols, specifically regarding use of varying energy levels, the

number of treatments needed, and intervals at which treatments are given. From all of the studied indications, most variability is seen with the treatment of acne and scarring. Greater consistency was seen in venous ablation where only one session was needed in all studies. Long term follow-up beyond five years would bolster the promising safety and efficacy profile of RF demonstrated so far. Additional studies with larger sample sizes are needed to better correlate clinical findings with molecular and tissue level changes, appropriately expand non-invasive indications, and streamline delivery method for RF.

#### Conclusion

Treatment with RF is an effective minimally invasive modality. Its use in non-cosmetic cutaneous conditions is beneficial for its short post-procedure recovery time, infrequent severe adverse events, and non-inferior rates of relapse for up to five years post-treatment in certain conditions. This review furthers an ongoing discussion of the utility of this technology in dermatology. Although these studies provide valuable information, better designed studies with increased sample sizes and longer follow up protocols are needed to make definitive recommendations about RF treatment.

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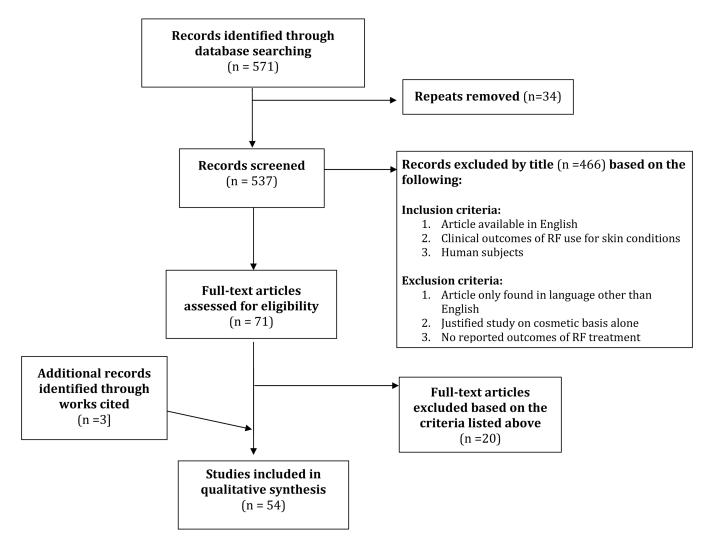
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**Figure 1.**Summary of article selection for clinically relevant reports of radiofrequency treatment for non-cosmetic dermatologic conditions

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Table 1.

Reports of radiofrequency treatment of acne and acne scarring

Adverse events	Transient pain, erythema, edema, effusion, and scabs in all pts	Mild pain, erythema, and edema FMR > BR (% not reported)	Mild erythema 84% 1° facial burns 12%	Erythema FMR: 2.35 ± 1.04 CO <sub>2</sub> FS: 1.75 ± 12.67 (p<0.001) Transient hyperpigmentation in 2 CO <sub>2</sub> FS pts
Patient Reported Outcomes	Patient satisfaction: 100% were "satisfied" or "very satisfied" with treatment at 6 months	Patient satisfaction: BR > FMR on day 1 FMR > BR on day 84	Patient-reported improvements: Excellent 4.5% Good 59% Very good 32% None to mild 4.5%	Patient Satisfaction at 3 months: Very satisfied 15% Satisfied 55% Sightly satisfied 10% Unsatisfied 5%
Clinical Outcomes	Avg ECCA score at 6 months: 107.2 at baseline, decreased to 42.27 (p<0.05)	Lesion count FMR Baseline 100 3 months 19.6 (p<0.001) BR Baseline: 100 3 months: 84.5 (p>0.001)	Avg reduction in lesion count: 47% (p<0.05)  Perifollicular lymphocytic infiltrates: Baseline: 58% 1-month: 33%  Avg area of sebaceous glands: Baseline: 0.092 mm² 1-month: 0.070 mm²	GIS at 3 months: FMR: 2.3 CO <sub>2</sub> FS: 1.9 (p>0.05) Lesion count 3 months: FMR: 36% reduction CO <sub>2</sub> FS: 41% reduction (p>0.005)
Outcome Measures	Echelle d'Evaluation Clinique des Cicatrices d'Acne (ECCA grading scale)	Inflammatory lesion count	Lesion count Histology Patient-reported improvement	Global Improvement Scale (GIS) (0 = worsening; $4 = 76 - 100\%$ improvement) Inflammatory lesion count
Number of Treatments/ Intervals	1 session q2 months x3	2 sessions q4 weeks x3	2 sessions q- week x4	1 – 2 sessions
Intervention	Micro-plasma radiofrequency	Bipolar radiofrequency (BR) Fractional microneedling radiofrequency (FMR)	RF and pulsed light combination	FMR Fractional carbon dioxide laser therapy (CO <sub>2</sub> FS)
Condition	Acne scarring	Acne and acne scarring	Acne	Acne
Study Design (Sample Size)	Prospective nonrandomized (n = 86)	Prospective single-blind randomized split-face trial (n = 20)	Case Series (n = 32)	Prospective single-blind randomized split-face trial (n = 20)
Evidence	.8	2	4	2
Author Publication Year	Lan et al. 2018 (11)	Min et al. 2015 (9)	Prieto et al. 2005 (10)	Shin et al. 2012 (8)

Table 2.

Reports of radiofrequency treatment of primary axillary hyperhidrosis

St De Cyidence (Sa Si	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
Single blind sham control (n = 25)		Primary axillary hyperhidrosis	FMR w/ topical anesthesia	1 session q3 weeks x3	HDSS Sweating visual analogue scale (VAS) Pre and post histology	HDSS: Baseline: treated 3.46; control 3.46 5 months: treated 1.87; control 3.38 (p=<0.001) VAS: Baseline: treated 9; control 9 5 months: treated 3.92; control 8.44 Histology changes: Sweat gland necrosis Mild inflammatory cell infiltrate	Patient satisfaction: 80% of pts reported more than 50% satisfaction	Erythema 68% Pinpoint bleeding 56% Hyperpigmentation 44% Tingling 1 pt
Case report (n = 1)		Primary axillary hyperhidrosis	FMR	1 session q2 weeks x4	Starch-iodine test	Starch-iodine: Pretreatment positive Post treatment negative	No hyperhidrosis at 6-months	Skin irritation, erythema, and pin-point bleeding
Case series (n = 20)	1	Primary axillary hyperhidrosis	FMR w/ tumescent anesthesia	1 session q4 weeks x2	Hyperhidrosis Disease Severity Scale (HDSS): 4-point scale (1– 4) Starch-iodine test Histologic analysis	HDSS: Baseline: 3.3 4 weeks after 1st treatment: 1.5 8 weeks after 2nd treatment: 2.3 (p<0.001) Starch-iodine test: Decreased area in 95% of subjects Histology: Decreased density and size of sweat glands	Patient satisfaction: (10 "no improvement"- 4 ">75% improvement"): 4 weeks after 1st treatment: 3.3 4 weeks after 2nd treatment: 3.0 8 weeks after 2nd treatment: 3.0	Temporary tingling, swelling and erythema in all pts Compensatory hyperhidrosis in 2 pts and transient numbness in 1 pt
Case series (n = 30)	1	Grade III axillary hyperhidrosis	FMR w/ local anesthesia	1 session q6 weeks x3	HDSS Dermatology Life Quality Index (DLQI)	HDSS: Baseline: 3.5 5 months 2.1 (p<0.05) DLQI: Baseline: 16 5 months: 7 (p<0.05)	Patient satisfaction: Satisfied 53% Very satisfied 37% Average reduction 72%	Petechial bleeding 50% Am twitching during treatment 27% Erythema 100% Ulceration 7% Post anesthesia pain 70%

Table 3.

Reports of radiofrequency treatment of wounds

Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse
Conner-Kerr and Isenberg et al. 2012 (16)	4	Case series (n = 89)	Chronic pressure ulcers (majority on sacrum and ischium)	Pulsed RF Energy (PRFE)	30-minute treatments BID x 4 weeks	Percent wound surface area reduction (PWAR) Wound healing	PWAR: 51% median reduction (p<0.0001) Wound healing: Baseline median size 9.8cm² At 4 weeks median size	Not reported	Not
Frykberg et al. 2011 (17)	5	Case report $(n = 1)$	Transmetatarsal amputation wound due to necrotizing fasciitis	RRFE w/ negative pressure and dermal replacement	BID x 14 weeks	Wound healing	Wound healing: Complete closure at 39 weeks	Not reported	Fixed equinus deformity
Larsen et al. 2008 (18)	4	Case series (n = 2)	Case 1: 1.75cm² diabetic foot ulcer Case 2: 7cm² transmetatarsal amputation dehiscence	RRFE w/ Case I: splint, cane, debridement, silver dressings, petroleum jelly Case 2: silver dressings, debridement, and rook boot.	Not reported	Wound	Wound healing: Case 1 and 2 complete closure at 16 weeks; closed at 9 and 7 month follow up, respectively	Not reported	Not
Maier et al. 2011 (5)	4	Case series (n = 2)	Case 1: Lower extremity ulcers due to thromboses Case 2: Lower extremity ulcer due to scleroderma	RRFE placed over compression wrapping	30-minute treatments BID x 2 weeks	Pain level Wound healing	Pain level: Both able to tolerate compression dressings again  Wound healing: Case 1 complete closure in 3-4 weeks Case 2 80% closure in 11 weeks	Immediate pain reduction	Not

Table 4.

Reports of radiofrequency treatment of cutaneous neoplasms

_s		ıt				b, y	f	(1-	ions:
Adverse events	None reported	Pt did not have scarring or pigment changes	Not reported	Not reported		1 pt with erythema, hyperpigmentation.	and scarring	Mean pain score during procedure (1–10): Vascular Iesions: 3.11	Non-vascular lesions: 3.95
Patient Reported Outcomes	None reported	Not reported	Not reported	Not reported		Patient satisfaction:	100%	Patient satisfaction: Vascular lessions: 94.4% very satisfied 5.6% satisfied	Nonvascular lesions: 83.9% very satisfied
Clinical Outcomes	VAS at 6 months: 70% for trichoepitheliomas 100% for cylindromas Recurrence: none at 6 months	Recurrence: Small lesions at 3 months	<b>Lesion size:</b> Decreased by 50%	Lesion size: Total clearance in all cases  Recurrence: None at 6 months or 2-	3 years	Duration of surgical procedure Avg 2 hours Re-epithelialization	time: Face: avg 1.5 weeks Trunk/Extremities: avg 2.5 weeks	Clinical outcones: Vascular Lesions: Excellent: 33.3% Good: 44.4% Moderate: 11.1% Poor: 11.1%	Non-Vascular Lesions: Excellent: 48.3% Good: 45.2% Poor: 3.2% (lentigo)
Outcome Measures	Efficacy of treatment VAS Recurrence	Recurrence	Lesion size	Lesion size Recurrence		Duration of surgical procedure	Re- epithelialization time	Clinical outcomes: 1) Excellent: Complete resolution 2) Good: 75%	3) Moderate: >50% reduction 4) Poor: < 50% reduction reduction
Number of Treatments/ Intervals	15 sessions	1 session	1 session	1 session monthly x1-4		1 session		1 session	
Intervention	RFA	RFA followed by dermal abrasion	RFA	RF w/ 3% polidocanol sclerotehrapy		RFA followed by excision w/	general anesthesia	27.12 MHz RF w/o	
Condition	Brooke-Spiegler Syndrome	Facial angiofibromas due to tuberous sclerosis	Dermatofibrosarcoma protuberans (DF) (20×10cm)	Angiolymphoid hyperplasia w/ eosinophilia		Neurofibromatosis type I		Telangiectasias (n = 22) Angioma (n = 15) Seborrheic Keratosis (n = 8) Skin Tags (n = 13) Lentigo (n = 1)	Precing hole $(n = 1)$ Acne $(n = 2)$ Dilate pore $(n = 2)$ Milium $(n = 2)$
Study Design (Sample Size)	Case report (n = 1)	Case report (n = 1)	Case Report (n = 1)	Case series (n = 3)		Case series (n =	16)	Case Series (n	
Evidence	4	4	4	4		4		4	
Author Publication Year	Chaudhary et al. 2012 (20)	Gomes et al. 2011 (6)	Imai et al. 2004 (23)	Khunger et al, 2010 (19)		Kim et al.	2013 (21)	Kim et al. 2016 (22)	

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Adverse events		
Patient Reported Outcomes	16.1% satisfied	
Clinical Outcomes		
Outcome Measures		
Number of Treatments/ Intervals		
Intervention		
Condition		
Study Design (Sample Size)		
Evidence		
Author Publication Year		

Table 5.

Reports of radiofrequency treatment of lymphangioma circumscriptum (microcytic lymphatic malformation)

Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
Niti et al. 2010 (24)	7	Case series (n = 14)	ГС	Group A: RFA w/ sclerotherapy Group B: Sclerotherapy	Group A: 1– 12 sessions, monthly Group B: 1 treatment	Lesion surface area Recurrence rate	Lesion surface area: RFA: 88.5% reduced in 90% of pts Sclerotherapy: 56% Recurrence rate: RFA at 6–60 months: 60% Sclerotherapy at 2 years: 25%	Patient-reported efficacy: RFA: Average of 2.2 months for resolution of all symptoms Sclerotherapy: 50% of patients with symptom resolution	Focal superficial scars and transient hypopigmentation 100% Persistent induration 30% RFA pts Ulceration 40% RFA pts
Khurana et al. 2018 (25)	4	Case series (n = 1)	TC	RFA w/ bleomycin sclerotherapy and local anesthesia	1 session monthly x3	Lesion recurrence	Lesion recurrence at 6 months: None, except a few vesico-papules near periphery	Not reported	Hypopigmentation of scar
Lapidoth et al. 2006 (26)	4	Case series (n = 6)	TC	RF w/ 900nm diode laser and local or general anesthesia	1 – 3 sessions	Lesion clearance (5-point scale; excellent (75– 100%), poor (<25%), worse)	Lesion clearance at 2 months: Excellent: 66.6% Good: 33.3% Fair, poor, or worse: 0%	Not reported	Transient swelling, pain, erythema all pts Ulcers and scarring 1 pt Hypopigmentation 1 pt
Hm et al. 2008 (27)	4	Case series (n = 2)	TC	RF	1 session	Lesion remission	Lesion remission: Pt 1: resolved w/ atrophic scar Pt 2: partial resolution w/ no scarring	Not reported	Atrophic scarring 1 pt
Sachdeva et al. 2011 (28)	4	Case report (n = 1)	TC	RF w/ local anesthesia and topical antibiotic	1 session weekly x3	Lesion reduction Lesion recurrence	Lesion reduction at 1 month: Complete resolution Lesion recurrence at 1 year: None	Not reported	Depigmentation (resolved at 3 months)
Subhadarshani et al. 2018 (29)	4	Retrospective cohort (n = 9)	TC	RFA w/ local anesthesia (2% lidocaine)	1-8 sessions	Global Assessment Scores (GSA) (0–10)	Physician GSA at 2–36 months: Avg 7.33 (2.49 SD)	Patient GSA at 2-36 months: Avg 7.55 (2.71 SD)	Hypertrophic scar at cannula entry 22% Transient edema 100%

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Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
					Oral LC				
Civelek et al. 2012 (30)	4	Case report (n = 1)	Lymphangioma circumscriptum (LC)	BR w/ surgical excision	1 session q4–8 weeks x2	Lesion size	Lesion size: Reduced by 50%	Patient satisfaction: Reduction with RFA alone was not satisfactory	Not reported
Grimmer et al. 2006 (31)	4	Case report (n = 11)	Oral L.C.	RF	1 session	Antibiotics Symptom reduction Postoperative oral intake	Antibiotics: Reduced Symptom reduction: 54% w/ significant reduction 9% w/ complete resolution Recovery room oral intake: 64%	Patient satisfaction: 62% of parents reported treatment being better than previous treatments	Not reported
Kim et al. 2011 (32)	4	Case series (n = 26)	Oral L.C.	RFA	1 – 7 sessions	Symptom	Symptom at 3 months: 18/26 pts controlled 13/26 pts w/ resolved symptoms after 1 session	Patient satisfaction: 21/26 satisfied with outcome of treatment	Intermittent bleeding 3 pts Persistent infections 1 pt Tongue edema 1 pt
Ryu et al. 2008 (33)	4	Case report (n = 1)	LC of the tongue	Lower power RFA	1 session monthly x2	Symptom	Symptom control: Complete symptomatic relief at 2 months; no recurrence at 1 year	Patient satisfaction: Complete symptomatic relief at 2 months post treatment	Pt reported to have none

Table 6.

Reports of radiofrequency treatment of cutaneous leishmaniasis

Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
Bumb et al. 2013 (36)	2	RTC (n = 100)	Cutaneous Leishmaniasis	Group A: RF w/ 1% lidocaine HCl Group B: Intralesional sodium	Group A: 1 session Group B: 1	Cure rate Recurrence	Cure rate at 6 months: RF Group: 98% SSG Group: 94% (P > 0.05) Recurrence:	Not reported	Not reported
				stibogluconate (ILSSG)	injection twice weekly x7		At 12 months: 0% At 18 months: 56% RF group; 54% SSG group		
				Group A: RF	Group A: 30 second session q7 days x3		Re-epithelialization at 13 weeks: RF:73%		Antimony: Keloid 1 pt
Navin et al.	2	RTC (n = 66; RF n =	Cutaneous Leishmaniasis	Group B: IM injection of nentavalent	Group B: 30 sec	Re- epithelialization	Antimony: 73% Placebo: 27%	Not	Abnormal amino transferase 1 pt
		22)		antimony Group C: Placebo	Group C: 30 second session q7 days x3	Recurrence	Recurrence at 9 months: RF: 6.3% Antimony: 12.5% Placebo: 0%		RF: Keloid 2 pts Cellulitis 4 pts
Reithinger et	·	RTC (n =	Cutaneous	6.78 mHz RF for 30 seconds w/ 1% lidocaine HCl	•	Cure rate	Cure rate: RF: 69.4% ILSSG: 75.3% IMSSG: 44.8%	Not	Secondary infection
al. 2005 (35)	٧	259)	Leishmaniasis	IL.SSG Intramuscular SSG (IMSSG)	ı neament	Median time to cure	Median time to cure: RF: 53 days ILSSG: 75 days IMSSG: >100 days	reported	o Mr pus 5 ILSSG pts 2 IMSSG pts
				,			Cure rate at 6 months: RF 80.7% Meglumine: 55.3%		Group A Satellite lesions in 1 case
Sadeghian et al. 2006 (37)	Н	RTC (n = 117)	Cutaneous Leishmaniasis	Group A: Kr Group B: Intralesional meglumine	Group A: 1 session weekly x4 Group B: weekly x4	Cure rate Scar diameter	Mean diameter of scar: RF baseline: 15 mm; 6 months: 14.8 mm (p=0.83)	Not reported	Group B Erythema, edema and pruritus in 4 patients
				anumomate			Meglumine baseline: 15.9mm; 6 months: 11mm (p<0.05)		Sporourchold lesions in 4 cases Satellite lesions in 3 cases
Velasco- Castrejon et al. 1997 (38)	4	Case series (n = 201)	Cutaneous Leishmaniasis	Localized current field radio frequency (LCF-RF)	1 session (n = 190)	Cure rate	Cure rate at >8 weeks: 90% had completely cured	Not reported	Not reported

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Adverse events		
Patient Reported Outcomes		
Clinical Outcomes		
Outcome Measures		
Number of Treatments/ Intervals	2 sessions (n = 11)	
Intervention	w/ 1% lidocaine HCl	
Condition		
Study Design (Sample Size)		
Evidence		
Author Publication Year		

Table 7.

Reports of radiofrequency treatment of non-acne scarring

	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse
4	4	Case series (n = 2)	Skin graft contraction	Micro-plasma RF w/ 10% Iidocaine cream	1–2 sessions	Scar contraction and dyspigmentation	Scar contraction at 6 months Scarred skin matched surrounding skin	Not reported	Not reported
4	4	Prospective case series (n = 4)	Hypertrophic scars	FMR w/ acoustic pressure ultrasound	l session q3-4 weeks x1-4	Complete	Complete resolution 75%	Not reported	Burning, erythema, and edema in all pts Fine scale and mild atrophy in 1 pt
4	4	Case series (n = 20)	Scars (various etiology)	FMR w/ topical anesthetic	1-4 sessions	Clinical efficacy (1–10 scale)	Clinical efficacy Avg 6.25/10 (± 1.5)	Patient-rated efficacy Avg 5.8/10 (± 1.8) Patient satisfaction Avg 7/10 (±1.6)	Erythema in 60% Scabs in 45% Edema in 45%
4	4	Case report (n = 1)	Hypertrophic burn scars	Monopolar radiofrequency (target temp above then below 40°C)	5 sessions	Histology (% collagen)	Histology (% collagen) Normal skin: 30.0 5% Hypertrophic scar: 30.62 % (p>0.05) w/ RF 40°C: 29.26 % w/ RF 40°C: 49.44 % (p>0.05)	Not reported	Not reported
- 4	4	Case report (n = 1)	Nasolabial necrosis scar	RF w/ pneumatic needleless injector	5–10 minute session monthly x6	Physician reported improvement	Clinical improvement: Significant	Not reported	Not reported
4	4	Case series (n = 14)	Hypertrophic and atrophic scars	FMR w/ acoustic pressure ultrasound and topical lidocaine	I session q3 weeks x6	Scar severity (1–6 scale) Scar attenuation Histology	Severity: Baseline: 4.12 At 6 months: 2.55 (P<0.0001) Scar attenuation: Avg 67% Histology	Patient satisfaction: Very satisfied: 7 Satisfied: 4 Somewhat satisfied: 1 Dissatisfied: 1	Erythema, edema, and fine scabs (% not reported)

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Adverse events				
Patient Reported Outcomes				
Clinical Outcomes	increased collagen	Hvpertrophic	scars: resolved	bsendonodules
Outcome Measures				
Number of Treatments/ Intervals				
Intervention				
Condition				
Study Design (Sample Size)				
Evidence				
Author Publication Year				

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Table 8.

Reports of radiofrequency treatment of varicose veins

Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
Dunn et al. 2006 (45)	6	Prospective nonrandomized (n = 68; 85 extremities)	Incompetent GSV	Endovenous radiofrequency ablation (ERA) w/tumescent anesthesia and sedation	1 session	Duplex ultrasound (DUS) Occlusion	Occlusion rate: 96% at 3 days 90% at 6 months Overall success rate: 88% at 6 months	Not reported	At 3 days (n=83): Ecchymosis 13% Erythema 13% Hematoma 2% Hyperpigmentation 1 pt At 6 months (n=73): Hyperpigmentation 3% Paresthesia 4%
Garcia- Madrid et al. 2013 (46)	3	Prospective nonrandomized (n = 59; 67 extremities)	Incompetent GSV	ERA w/ tumescent anesthesia	1 session	DUS Occlusion	Occlusion rate: 100%	Not reported	Erythema 1 pt Class 1 heat-induced thrombosis 1 pt
Gibson et al. 2017 (47)	-	Randomized control trial (n = 222)	Incompetent GSV	Cyanoacrylate closure (CAC) w/o anesthesia Radiofrequency ablation (RFA) w/tumescent anesthesia	1 session	DUS Occlusion Symptoms	Occlusion rate At 1 year: RFA 97.0% CAC 97.2% At 2 years: RFA 94.0% CAC 95.3%	Patient satisfaction at 2 years: REA 75% CAC 79.1%	At 12–24 months: Pain (RFA 21%; CAC 30%) Aching (RFA 34%; CAC 29%) Heaviness (RFA 14%; CAC 13%) Swelling (RFA 16%; CAC 16%)
Mallick et al. 2016 (48)	4	Retrospective cohort (RF n = 7,355; total n = 144,098)	Incompetent GSV	RFA Sclerotherpy Laser ablation	1 session	Rates of new venous ulcers Rates of additional interventional treatment Disease progression	New venous ulcers at 1 year: RF 2.4% Sclerotherapy 1.2% Laser ablation 2.2% Additional treatment sought at 1 year: RF 53.3% Sclerotherapy 63.6% Laser ablation 66.8% Disease progression at 2 years: RF 42.4% Sclerotherapy 28.6% Laser ablation 37.8%	None collected	Not reported
Mendes de Almeida et al. 2016 (49)	-	Randomized, controlled trial (n = 18)	Incompetent GS V	ERA in one leg and conventional surgery in the	1 session	DUS occlusion Reflux sapheno-	<b>DUS Occlusion:</b> 8/10 (80%) at 12 months	Patient satisfaction at 6 months	Not reported

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Author Publication Year	Evidence	Study Design (Sample Size)	Condition	Intervention	Number of Treatments/ Intervals	Outcome Measures	Clinical Outcomes	Patient Reported Outcomes	Adverse events
				other; both w/ spinal anesthesia		femoral junction (SFJ) and GSV	Reflux SFJ: 0/10 (0%) at 12 months Reflux GSV: 0/15 (0%) at 12 months	(1–10): CS 6.93±2.70 RPA RPA Pain at 6 months (1– 10): CS 5.64±3.80 RFA 3.71±3.27	
Proebstle et al. 2011 and 2015 (57–58)	m	Prospective nonrandomized (n = 225, 295 extremities)	Incompetent great saphenous vein (GSV)	Radiofrequency segmental thermal ablation (RSTA)	l session	DUS Occlusion Venous Clinical Severity Score (VCSS)	<b>DUS Occlusion:</b> 92.6% at 3 years 91.9 % 5 years 11.9 % 5 years <b>Avg VCSS:</b> Baseline: 3.9 ±2.1 3 years: 0.9 (p=0.05) 5 years: 1.3 <b>Pain:</b> Baseline 17.3% w/daily pain 3 years: 1.4% w/daily pain 5 years: 2% w/daily pain	None collected	1 Week: Ecchymosis 5.8% Paresthesia 3.4% Pigmentation 2.4% Erythema 2.% 3 years: Leg hyperpigmentation 1 pt Persisting paresthesia 1 pt 5 years:
Schuller- Petrovic et al. 2016 (50)	4	Retrospective cohort (n = 258; 389 extremities)	Incompetent GSV and superficial saphenous vein (SSV)	RSTA	1 session	DUS Occlusion	DUS at 5 years: 78.5% GSV 58% SSV	Not Reported	Hypesthesia 1% Hyperesthesia 2% Ecchymoses 4% Phlebitis 4% Deep vein thrombosis 6%
Spiliopoulos et al. 2015 (51)	4	Prospective case series (n = 60; 74 extremities)	Incompetent GSV and SSV	ERA w/ tumescent anesthesia	1 session	CEAP Classification (C0 clinical best - C6 clinical worst) VCSS Revascularization rate	Clinical success: 94.6% improvement Baseline: 72.9% C2-C3 At 1 year: 12.1% C2-C3 VCSS: baseline: 6.2±2.6 I month: 1.3±1.2 I year: 0.9±1.4 P<0.0001  Revascularization rate 12.1%	Not reported	Puncture site infection 1 pt Transient paresthesia 2 pts Puncture site scar 2 pts Skin pigmentation 1 pt
Tolva et al. 2012 (52)	4	Case series (n = 407)	Incompetence GS V	ERA w/ spinal anesthesia	1 session	DUS Occlusion	Occlusion rate: 100% at 1 week and 6 month follow ups	Not reported	Thrombophlebitis 3 pt Skin pigmentation 1 pt Paresthesia 1 pt

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Adverse events	Nonocclusive thrombus 1 pt	Not reported, except no hospitalizations for procedure-related complications	Superficial thrombophlebitis (12%) Ecchymosis (13.1%) Erythema (2.5%) Infection (0.5%) Paresthesia (0.3%)	Worsening of leg swelling: 1 pt Localized thrombophlebitis: 2 pts. Acute nonocclusive thrombus extending to the common femoral vein from GSV: 1 pt	Not reported
Patient Reported Outcomes		Not reported	Patient satisfaction: 98%	Patient satisfaction at 2 years: 94.5%	Not reported
Clinical Outcomes		Occlusion rate (1 year): 87%	VCSS: Baseline 8.8 At 1 year 3.6 Occlusion rate at 1 year: 87.1% Symptoms: Pain reduced from 95.7% to 15.2% (p < 0.0001) Gleena reduced from 92.4% to 17.0% (p < 0.0001) Stasis ulcers healed at rate of 86%	Occlusion rate: 100% at 1 year	Occlusion at 5 years: RFA 61.7% ND:YAG 84.7% Diode laser 65.7% (P<0.0001)
Outcome Measures		DUS Occlusion	VCSS Occlusion rate Symptoms	DUS Occlusion	DUS Occlusion
Number of Treatments/ Intervals		1 session	1 session	1 session	1 session
Intervention		ERA w/ regional or general anesthesia or tumescent anesthesia	ERA w/ tumescent anesthesia	ERA w/ general anesthesia	ERA w/ tumescent anesthesia 1.320mm ND: YAG w/ tumescent anesthesia 810nm Diode (n = 34)
Condition		Incompetent GSV and SSV	Incompetent GSV	Incompetent GSV	Incompetent GSV and SSV
Study Design (Sample Size)		(n = 421; 490 extremities)	Prospective cohort (n = 499; 682 extremities)	Retrospective cohort (n = 24; 28 extremities)	Retrospective cohort (n = 934 extremities; ERA n = 398)
Evidence		4	.6	4	4
Author Publication Year		Tzilinis et al. 2005 (53)	Vasquez et al. 2007 (54)	Wagner et al. 2004 (55)	Weiss et al. 2015 (56)

 $w = with; \ pt = patient; \ q = every \ (i.e. \ q^2 \ weeks = every \ 2 \ weeks); \ x = times \ to \ repeat \ (i.e. \ x3 = repeat \ 3 \ times)$