Disclosure

- Medtronic – Consultant/ Speaker
- Bard – Data Safety Committee
- Volcano – Consultant
- Boston Scientific – Consultant/ Speaker
- Inari – Consultant
- Spectranetics – Consultant
- BTG – Consultant/ Research Grant
Venous Ulcers

• Most common chronic wounds in ambulatory elderly

• 60-70% of all Lower Extremity Wounds are VENOUS

• Profoundly decrease quality of life causing social isolation

We suggest using pentoxifylline or micronized purified flavonoid fraction, if available, in combination with compression, to accelerate healing of venous ulcers.

We recommend compression as the primary therapeutic modality for healing venous ulcers.

We recommend compression as an adjuvant treatment to superficial vein ablation for the prevention of ulcer recurrence.

To decrease recurrence of venous ulcers, we recommend ablation of the incompetent superficial veins in addition to compression therapy.
Long term results of compression therapy alone versus compression plus surgery in chronic venous ulceration (ESCHAR): randomised controlled trial

Manjit S Gohel, specialist registrar,¹ Jamie R Barwell, consultant vascular and transplant surgeon,² Maxine Taylor, leg ulcer nurse specialist,¹ Terry Chant, vascular nurse specialist,³ Chris Foy, medical statistician,⁴ Jonothan J Earnshaw, consultant surgeon,⁵ Brian P Heather, consultant surgeon,⁵ David C Mitchell, consultant surgeon,³ Mark R Whyman, consultant surgeon,¹ Keith R Poskitt consultant surgeon¹

BMJ. 2007 Jul 14;335(7610):83
The Role of Superficial Venous Surgery in the Management of Venous Ulcers: A Systematic Review

D.P.J. Howard a,*, A. Howard b, A. Kothari a, L. Wales c, M. Guest c, A.H. Davies c

Table 1: Results of recent RCTs comparing superficial venous surgery to compression therapy for treatment of venous ulcers

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Date published</td>
<td>2003</td>
<td>2003</td>
<td>2007</td>
<td>2006</td>
</tr>
<tr>
<td>Treatment (Sx/Cx)</td>
<td>Sx</td>
<td>Sx</td>
<td>Sx</td>
<td>Sx</td>
</tr>
<tr>
<td>Number of legs</td>
<td>37</td>
<td>21</td>
<td>242</td>
<td>93</td>
</tr>
<tr>
<td>VU healed (%)</td>
<td>68</td>
<td>100*</td>
<td>93</td>
<td>83</td>
</tr>
<tr>
<td>VU recurrence (%)</td>
<td>N/a</td>
<td>9*</td>
<td>31*</td>
<td>22</td>
</tr>
<tr>
<td>Ulcer-free rate (%)</td>
<td>N/a</td>
<td>N/a</td>
<td>78*</td>
<td>72*</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>6.5</td>
<td>36</td>
<td>36 &amp; 48</td>
<td>29</td>
</tr>
</tbody>
</table>

Sx, superficial venous surgery; Cx, compression therapy without surgery; *, statistically significant result; N/a, not assessed.
The impact of ablation of incompetent superficial and perforator veins on ulcer healing rates

Michael Harlander-Locke, a Peter F. Lawrence, MD, b Ali Alktaifi, MD, b Juan Carlos Jimenez, MD, b David Rigberg, MD, b and Brian DeRubertis, MD, b San Diego and Los Angeles, Calif

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Compression Used</th>
<th>Followup Time</th>
<th>Ulcer Healing in Group 1, N / N (%)</th>
<th>Ulcer Healing in Group 2, N / N (%)</th>
<th>Relative Risk, Risk Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rojas, 2009</td>
<td>Unclear</td>
<td>Compression</td>
<td>Sclerotherapy - saphenous vein + perforator</td>
<td>Multilayer + Unna boot, 20-30 mmHg</td>
<td>21 weeks</td>
<td>23 / 37 (62%)</td>
<td>28 / 33 (85%); P=0.06</td>
<td>RR, 0.73 (CI, 0.55 to 0.98) RD, -23% (CI, -43% to -3%)</td>
</tr>
<tr>
<td>Galimberti 1988</td>
<td>Retrospective cohort</td>
<td>Compression</td>
<td>Sclerotherapy - saphenous vein + perforator</td>
<td>Class 3, 40-50 mm Hg</td>
<td>40 months</td>
<td>46 / 46 (100%)</td>
<td>72 / 72 (100%)</td>
<td>RR, 1 RD, 0</td>
</tr>
</tbody>
</table>

**Conclusion**

This trial failed to recruit sufficient patients for formal comparison, but foam sclerotherapy was feasible as an adjunct to compression therapy for venous ulceration. Trial registration: Eudra CT 2005-001551-38
Severe venous disease

- Pascarella et al
  - 60 limbs
    - CEAP 4 – 7
    - CEAP 5 – 18
    - CEAP 6 – 35
  - Group I – compression
  - Group II crossover patients who failed compression treatment
  - Group III sclerosant foam therapy

Severe venous disease

• Polidocanol 1%, 2%, or 3% - 2 syringe tech under US guidance

• Compression - 14 days.

• Limbs treated with foam had a statistically better outcome than those without (p = 0.041)
  • Healing 2-4 weeks (foam) Vs 6 weeks (compression only)

Healing & Recurrence – From SPAIN

- 180 VLU treated with USG polidocanol
- Median follow-up - 30 months
- 172 (95.6%) ulcers healed during the study
- 1,2,3 year ulcer recurrence - 8.1%, 14.9%, and 20.8%,
USGS sclerotherapy - From Brazil

- 87 patients - C5 and C6
- Ulcer healing (85%)
- Significant improvement of symptoms after treatment, such as pain, heaviness, fatigue, burning, paresthesia, and itching (P < 0.0001).

Phlebology. 2015 Mar;30(2):113-8
Current status/ Guidelines - Issues

- Only treatment shown to improve venous ulcer healing is compression bandaging.
- Poorly tolerated by some patients
- What about cost savings with earlier treatment of pathology?
- QOL and Pain with VLU – Pretty significant -> ? Early intervention justified?
Issues with foam sclerotherapy data

- Heterogeneity
  - Study design
  - Endpoints
    - % Healing Vs Time to heal Vs % Recurrence Vs Other patient reported outcomes
  - Ulcer healing
    - Measurement tools
    - Definition of closure

- BIGGEST ISSUE – FOAM COMPOSITION – HIGHLY VARIABLE!
What is Varithena®?

A Microfoam UDSS™ Procedure

UDSS = Uniform Density, Size, and Stability

A proprietary microfoam-generating canister produces a cohesive, low-nitrogen microfoam with a uniform density, bubble size, and stability.

< 0.8% Nitrogen Gas
1% Polidocanol Liquid
65:35 O₂:CO₂
Varithena® Administration Pack
Varithena® vs. PCF

DSS Method

Tessari Method

Varithena®

PCF

Graph showing dwell time (sec/cm) for RA, 65:35 O₂:CO₂, 35:65 O₂:CO₂, and Varithena®.
Only FDA approved foam rx in the USA
Effect of Polidocanol Endovenous Microfoam (PEM) Treatment of Superficial Axial and Tributary Vein Reflux on Improvement of Wound Healing in Venous Leg Ulcers (VLUs)

**Principal Investigator:** Raghu Kolluri, MD, RVT, FACC, FSVM  
Medical Director – Vascular Medicine  
OhioHealth Riverside Methodist Hospital  
3705 Olentangy River Rd., Columbus, OH 43214  
Phone: 614/262-6772  
Fax: 614/566-1286  
Raghu.Kolluri@ohiohealth.com

**Study Institution:** OhioHealth

**Study Sites:** Riverside Methodist Hospital  
Doctors Hospital

https://clinicaltrials.gov/ct2/show/NCT02988063?term=kolluri&rank=1
Study Details

- Prospective, single-arm trial, comparing VarithenaTM (polidocanol endovenous microfoam) plus compression therapy to the currently used compression-only treatment (run-in phase) to determine effectiveness in improving the healing of VLUs.

Pre-Screening (Clinic Staff):
1. Review schedule for potential patients
2. Notify OHRI-CRC of potential patients same-day (i.e., no advance screening taking place)

Preliminary Criteria:
a. VLU >4 weeks & <1 year
b. VIS+ GSV reflux

Screening (CRC):
1. Explain study
2. Determine interest
3. Provide consent form
4. Confirm eligibility
5. Schedule run-in compression phase (RMH or DH) for 4-5 weeks

Baseline “Day 0” (CRC):
1. Within 2 weeks of completion of run-in
2. Confirm non-healing ≤70% with run-in phase compression therapy
3. Re-confirm eligibility
4. Informed consent
5. SilhouetteStar wound measurement
Study Details

• Primary End point: Determine the change in ulcer healing rate following PEM treatment. Ulcer healing rate will be measured as the relative weekly change in ulcer perimeter from baseline, until either until fully healed, or up to the final active study visit at 12 weeks (whichever is sooner).

*Figure 2. Treatment Timeline.*
Study Details

- **Secondary endpoint**: Determine the proportion of patients who successfully heal by 12 weeks

- **Safety Endpoint**: Determine the proportion of patients who experience symptomatic PE and DVT and other drug-related adverse events (AEs) at 12 weeks (or the last active study visit if healed prior to 12 weeks)
### Table 2. Study Calendar.

<table>
<thead>
<tr>
<th></th>
<th>Screening</th>
<th>Week 1 (Baseline)</th>
<th>Day 4 (PEM only)</th>
<th>Week 2-12(^a) (Active) (+/- 2 days)</th>
<th>Week 24 (Follow-Up) (+/- 2 days)</th>
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<tbody>
<tr>
<td>Demographics &amp; History</td>
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<td>Venous Insufficiency S</td>
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<td>Run-In Phase (4-5 weeks)</td>
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<td>Consent &amp; Randomization</td>
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<td>RMH Critical Limb Cen</td>
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<td>Varithena™ Injection V</td>
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<td>SilhouetteStar(^b) Meas</td>
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<td>Duplex Imaging</td>
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<td>Adverse Events Assess</td>
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</table>
A randomised clinical trial to compare early versus delayed endovenous treatment of superficial venous reflux in patients with chronic venous ulceration.
Foam sclerotherapy and Polidoconol injectable foam for venous ulcerations

Raghu Kolluri, MD
System Medical Director – Vascular Medicine
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