Glue for the Treatment of Varicose Veins

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CAN IMPROVEMENTS BE MADE TO THERMAL ABLATION?

- Eliminate need for tumescent anesthesia
- Eliminate need for compression stockings
- Significantly reduce post-procedure pain and bruising

Images courtesy of M. Madsen
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NYU Langone Medical Center
Division of Vascular and Endovascular Surgery
CYANOACRYLATE USE: OCCLUSION

Adhesive cast in AVM delivered via micro catheter

Adhesive cast in AVM delivered via micro catheter

Image courtesy of Dr. R. Raabe
# ADHESIVES IN MEDICINE\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanoacrylate Adhesives</td>
<td>1950s</td>
<td>Wound adhesives</td>
</tr>
<tr>
<td>Histoacryl Blue(^\text{TM} \ast)</td>
<td>1980s</td>
<td>Skin incisions</td>
</tr>
<tr>
<td>Dermabond(^\text{TM} \ast)</td>
<td>1998</td>
<td>Skin incisions/lacerations</td>
</tr>
<tr>
<td>Ethicon OMNEX(^\text{TM} \ast)</td>
<td>1998</td>
<td>Surgical adhesives</td>
</tr>
<tr>
<td>Trufill(^\text{TM} \ast)</td>
<td>2000</td>
<td>Liquid Embolic System, AVM embolization</td>
</tr>
<tr>
<td>Indermil(^\text{TM} \ast)</td>
<td>2002</td>
<td>Skin incisions/lacerations</td>
</tr>
</tbody>
</table>

CYANOACRYLATE USE: OCCLUSION

- Vascular closing agent for
  - Cerebral Arteriovenous malformations (AVM)
  - Pelvic congestion syndrome and Varicoceles
  - Gastric varices
  - Aortic aneurysms
CYANOACRYLATE POLYMERIZATION STRUCTURE

Proprietary Formulation

Microscopic view of the polymerized adhesive

Proprietary formulation of advanced medical cyanoacrylate-based adhesive designed to coapt and close the vein
FIBROTIC CELLULAR GROWTH ACROSS THE LUMEN RESULTING IN PERMANENT OCCLUSION. FOREIGN BODY REACTION

Image courtesy of Dr. R. Raabe
INITIAL ANIMAL EXPERIMENT COMPLETED
6-25-09

Positive Study Objective: Complete Vein Closure in all tests 3/3
Venoseal (Cyanoacrylate Glue)
VENASEAL™ CLOSURE SYSTEM: PROCEDURE

VenaSeal™ Closure System

Access GSV using catheter technique

Position catheter 5 cm from SFJ

Compress cephalad to catheter
VENASEAL™ CLOSURE SYSTEM: PROCEDURE

1. Inject 0.10 cc adhesive into the vein, pull back 1 cm, inject 0.10 cc pull back 3 cm
2. Inject 0.10 cc, pull back 3 cm, compress for 30 seconds
3. Compress 3 minutes
4. Repeat process throughout vein
ULTRASOUND IMAGES 8 WEEKS POST TREATMENT

VenaSeal™ Procedure Closure

RFA Procedure Closure

Images courtesy of Dr. R. Raabe
Let’s Look at the Evidence
# Clinical Studies with the VenaSeal™ System

## Feasibility Study
- 38 Patients, enrollment completed Aug. 2011
- 1 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: Safety: rate of serious adverse events, Efficacy: vein closure during follow-up

## eSCoPE
*(European multicenter study)*
- 70 patients, enrollment completed Sept. 2012
- 2 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: closure w/o use of sedation, tumescent anesthesia or compression stockings

## VeClose
*(U.S. pivotal trial)*
- 242 patients, enrollment completed Sept. 2013
- 3 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: non-inferior to RFA in GSV closure
- Secondary endpoint: superiority in reduction of post procedural pain and bruising
VeClose \textit{(U.S. pivotal trial)}

- **Primary Endpoint**
  - Duplex ultrasound determined \textbf{closure} of the GSV, non-inferiority of VenaSeal™ closure system to ClosureFast™ (RFA)

- **Secondary Endpoints**
  - Intraoperative \textbf{pain}, rated on a 0-10 numeric rating scale
  - \textbf{Ecchymosis} at day 3, rated on a 0-5 ordinal scale
  - \textbf{Adverse events} at 1 month

- **Follow-up occurred at**
  - Day 3, and
  - 1, 6 and 12 months post-procedure

\textbf{No adjunctive therapy before 3 months}


Morrison N. Use Of Cyanoacrylate Adhesive For Treatment Of Incompetent Great Saphenous Veins: 12-month Results of the VeClose Trial. European Venous Forum. 2015
24 Month Results (VeClose)

VenaSeal Sapheon Closure System
vs.
Radiofrequency Ablation
Study Design

Enrolled (N=242)

Randomized (1:1) and Treated Subjects (N=222)

CAC (n=108) RFA (n=114)

Evaluation of perioperative parameters

Baseline Assessments Intraoperative pain Ecchymosis

Follow up at Day 3; and at 1, 3, 6, 12, 24, 36 months

Reevaluation of clinical assessments and adverse events

CAC Roll-In group Subjects (N=20)

### Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>CAC (N=108)</th>
<th>RFA (N=114)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.0</td>
<td>50.5</td>
<td>0.34</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>27.0</td>
<td>27.0</td>
<td>0.95</td>
</tr>
<tr>
<td>Mean GSV diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>6.3</td>
<td>6.6</td>
<td>0.15</td>
</tr>
<tr>
<td>Mid-thigh</td>
<td>4.9</td>
<td>5.1</td>
<td>0.28</td>
</tr>
<tr>
<td>Mean Treatment Length (cm)</td>
<td>32.8 (108)</td>
<td>35.1 (114)</td>
<td>0.17</td>
</tr>
<tr>
<td>Mean VCSS</td>
<td>5.5 ± 2.6</td>
<td>5.6 ± 2.6</td>
<td>0.99</td>
</tr>
<tr>
<td>Mean AVVQ</td>
<td>18.9 ± 9.0</td>
<td>19.4 ± 9.9</td>
<td>0.72</td>
</tr>
<tr>
<td>Mean EQ-5D TTO</td>
<td>0.935 ± 0.113</td>
<td>0.918± 0.116</td>
<td>0.29</td>
</tr>
</tbody>
</table>

### Primary Endpoint – Complete Closure

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Closure Rate CAC</th>
<th>Closure Rate RFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3</td>
<td>100% (108)</td>
<td>99.1% (114)</td>
</tr>
<tr>
<td>Month 1</td>
<td>100% (105)</td>
<td>87.3% (110)</td>
</tr>
<tr>
<td>Month 3</td>
<td>99% (104)</td>
<td>95.4% (108)</td>
</tr>
<tr>
<td>Month 6</td>
<td>99% (101)</td>
<td>96.2% (105)</td>
</tr>
<tr>
<td>Month 12</td>
<td>96.8% (95)</td>
<td>95.9% (97)</td>
</tr>
<tr>
<td><strong>Month 24</strong></td>
<td><strong>94.3% (87)</strong></td>
<td><strong>94% (84)</strong></td>
</tr>
</tbody>
</table>

94.3% closure rates, demonstrating continued non-inferiority to RFA (P=0.0075) thru 24 months
VCSS demonstrated statistically significant improvement out to Month 6 and sustained through 12M and 24M time points.
Subjects experienced statistically significant improvement over time, \( p<0.0001 \), but there was no difference between treatment groups.

**AVVQ:** a 13-question survey addressing physical symptoms, pain, ankle edema, ulcers, compression therapy use, and limitations on daily activities are examined, as well as the cosmetic effect of varicose veins and social issues.
24 Month - EQ5D Results

- EQ-5D was improved significantly from baseline at all time periods across all subjects.
- There was no difference in improvement of EQ-5D between randomization groups.

The EQ-5D includes single item measures of: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each item is coded using 3-levels (1 = no problems; 2 = some problems; 3 = severe problems).
Summary 24 months

- 94.3% closure rates=non-inferiority results to RFA
  - \( p=0.0075 \) at 24 months

- VCSS, AVVQ and EQ5D significant improvement
  - No difference between Rx Groups at 24 months

- Adverse events were extremely low in
  - The time period of 12-24 months across both treatment options
Biolas – Variclose Cyanoacrylate Adhesive (Turkey)
Long J wire in and US appearance
Priming of the catheter
Insertion and Connection
Pullback
Pulling back the catheter 3 cm to the SFJ
2\textsuperscript{nd} Generation CAA

- Automatic pull back
- Automatic dispenser
A prospective comparison of a new cyanoacrylate glue and laser ablation for the treatment of venous insufficiency

Ahmet Kürşat Bozkurt¹ and Muhammet Fatih Yılmaz²

The authors concluded that there was essentially clinical equipoise.