Rheological Characterisation of Sclerosing Foams in Biomimetic Settings Using Clinically-Relevant Parameters

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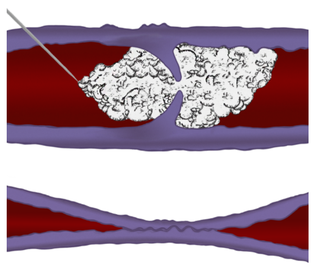
Introduction

Varicose Veins

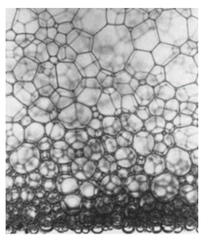
- **Twisted** and **dilated veins** ineffective at venous blood return.
- Extreme cases may cause **oedema** and **skin ulcers**.
- **Treatments**: Surgical removal or ablation (laser or chemical)
- One of the least invasive treatments is **sclerotherapy**.

Sclerotherapy



- Injection of a **surfactant solution** into the pathological vessels.
- The surfactant **reduces the surface tension** of endothelial cell membranes, causing **vascular sclerosis.**
- In larger vessels, the **sclerosant may deactivate and dilute with blood**. Therefore it is **injected as a foam**.

Ageing of Foams



Saint-Jalmes *et al.* (2006), *Soft Matter*, pp 836-849

- **Drainage** of the liquid phase is governed by gravity (downwards) and capillary (upwards) forces.
- **Coarsening** is governed by gas diffusion from smaller bubbles to bigger bubbles.
- **Coalescence** occurs as a result of rupture of the liquid films between large bubbles.

Rheology of Foams

- Aqueous **foams are shear-thinning** fluids.
- Due to the ageing phenomena, they exhibit a **time-dependent rheology**.
- History of shearing affects collected rheology data.
- In other words, **viscosity of foam is a function of time!**

Power-Law Model

- Describes non-Newtonian fluids
- Shear-thinning fluids exhibit $n < 1$
- Aqueous foams exhibit $0.2 \lesssim n \lesssim 0.5$
- Linear regression to obtain the indices

Fluid consistency index; Fluid flow index

$$\tau_w = K.(\dot{\gamma}_{obs})^n \quad \longrightarrow \quad \mu_{app} = K.(\dot{\gamma}_{obs})^{n-1}, \qquad \mu = \frac{\tau}{\dot{\gamma}}$$

Wall shear stress; Observed shear rate

$$\ln(\tau_w) = n.\ln\dot{\gamma}_{obs} + \ln K$$

Slope; Y-intercept

Knowledge Gap

- Despite removal the pathological vessels through treatment, varicosities **recur at rates of up to 64%** five years post-treatment (any treatment!).
- Recurrence is due to **neovascularisation**.
  - Neovascularisation: The formation of new blood vessels in response to ischaemia via migration of endothelial cells to regions experiencing ischaemia, resulting in a functional vascular network.
- Studies suggest that **varicose endothelium exhibits abnormal morphologies.**

Hypothesis

Improving the performance of the sclerosing foam may remove more "abnormal" endothelial cells and **reduce the chances of recurrence.**

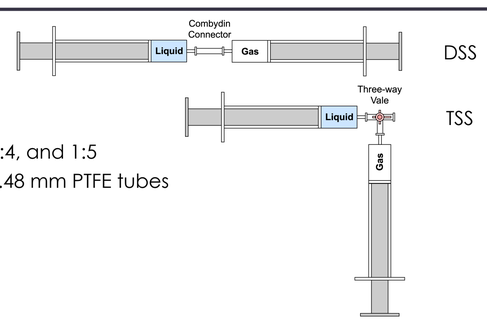
Validation

Characterise flow properties of sclerosing foams and **correlate with biological outcomes** of sclerotherapy in vitro and/or ex vivo.

Methodology

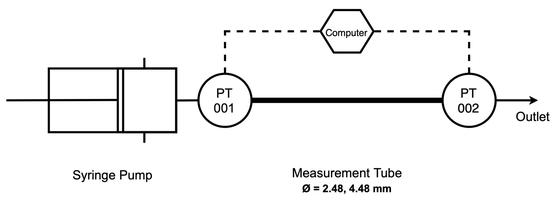
Experimental Parameters

- **1% Polidocanol** surfactant solution.
- 9 flowrates (**4 – 36 ml.min^{-1}**).
- 3 repeated measurements of P_{in} and P_{out} (n=3)
- 12 experiments:
  - **DSS** and **TSS** foams
  - Liquid-to-gas ratios of 1:3, 1:4, and 1:5
  - Vein model:2.48 mm and 4.48 mm PTFE tubes



Rheometry: Pipe Viscometry

- **Pipe viscometry to obtain rheograms (τ_w versus $\dot{\gamma}_{obs}$).**



Flowrate; Pipe diameter

$$\dot{\gamma}_{obs} = \frac{32\,Q}{\pi\,d^3}$$

Pipe diameter; Pressure difference; Pipe length

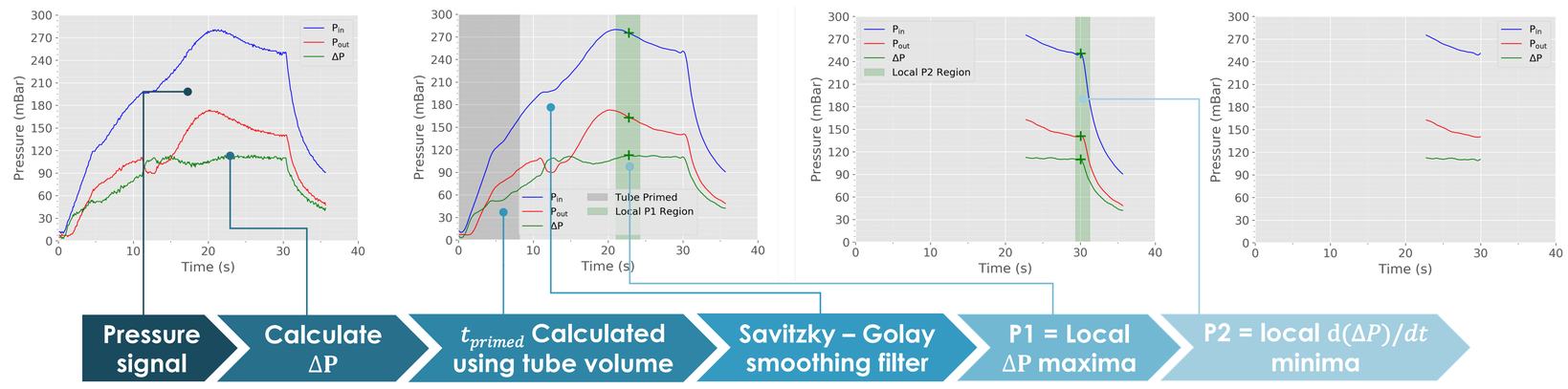
$$\tau_w = \frac{d\,\Delta P}{4\,L}$$

- Linear regression on log-transformed data ($\ln\tau_w$ and $\ln\dot{\gamma}_{obs}$) to obtain power law indices (n and K).

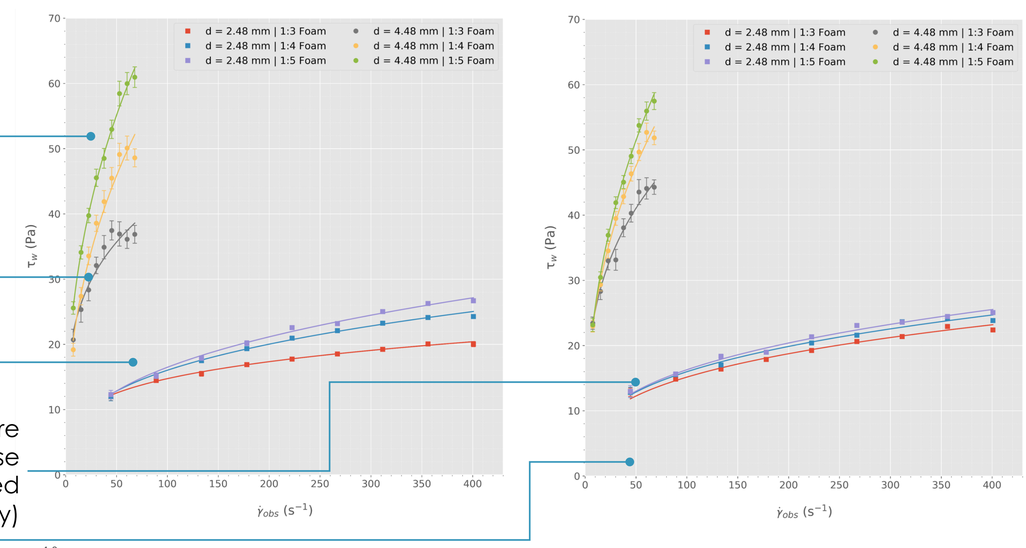
Effect of Vessel Size | **Effect of Foam Type**

Results

ΔP Plateau Detection



Rheograms



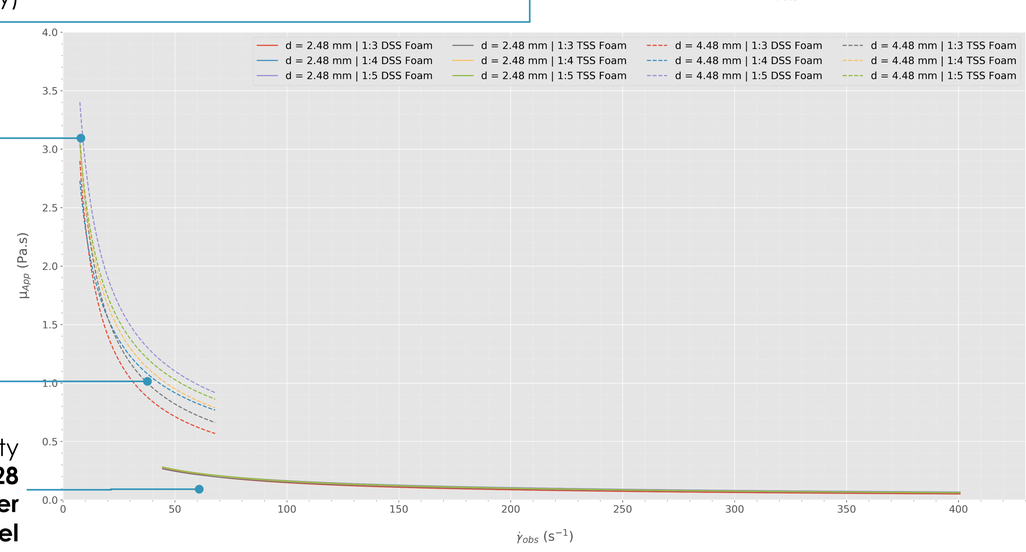
Larger vein model experienced greater viscosities

Greater measurement error in the large vein model

Viscosity increases with increasing foam dryness.

TSS foams are rheologically less diverse (curves are packed together more closely)

Consistent trends across different foam types (i.e. DSS versus TSS)



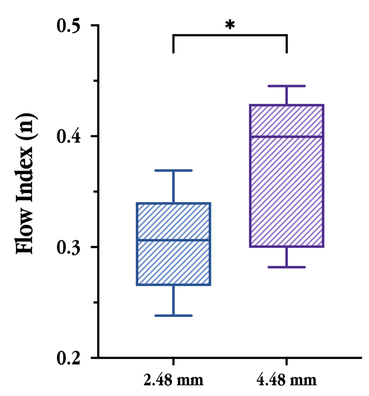
Apparent viscosity ranges **0.5 – 3.5 Pa.s** in the **larger vein model**

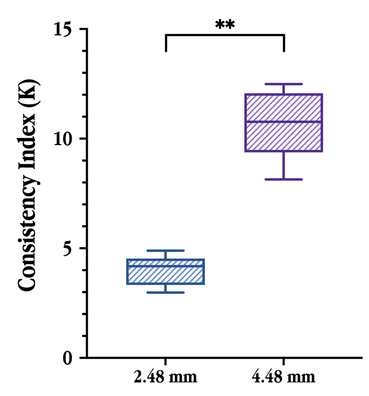
Apparent viscosity ranges **0.05 – 0.28 Pa.s** in the **smaller vein model**

Other studies employ **conventional rheometry** of sclerosing foams and report values **ranging 40 – 80 Pa.s!**

Power-Law Indices

- Non-parametric unpaired Mann-Whitney U-test to **evaluate the effect of vessel size:**
  - Statistically significant difference in observed foam rheology in vessels of different diameter.
  - Greater viscosities in the larger model reflected in greater K values.
- Two-way ANOVA to evaluate the **effects of formulation and liquid-to-gas ratio:**
  - Correlation between foam dryness and viscosity is statistically significant.
  - Wet (1:3) TSS foam is more viscous than wet (1:3) DSS foam ($P \leq 0.05$).
  - Dry (1:5) DSS foam is more viscous than dry (1:5) TSS foam ($P \leq 0.001$).





Conclusions

- This study employed **a biomimetic apparatus** to **evaluate the flow behaviour** of **sclerosing foams.**
- Different formulation techniques, liquid-to-gas-ratios and vessel diameters were tested.
- It was shown that foam viscosity depends strongly on vessel diameter.

Assumption: **Higher viscosity** leads **to better treatment outcomes.**

- When formulating wet foams, clinicians are suggested to employ the DSS technique.
- When formulating dry foams, clinicians are suggested to employ the TSS technique.
- In the future, the above assumption will be verified by administering different sclerosing foams on flow-cells seeded with HUVECs (human umbilical vein endothelial cells).
- In this future prospect, cell viability and treatment safety will be evaluated and correlated with foam rheology.

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