

# Non-invasive assessment of fluid retention in tissues by direct measurements of capillary parameters using optical microscopy

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# Diagnostic relevance of tissue's water content quantification

Edema syndrome (retention of fluid in tissues) is crucial to monitor in:

- **Reanimatology**: edema during infusions
- **Cardiology**: edema during heart failure

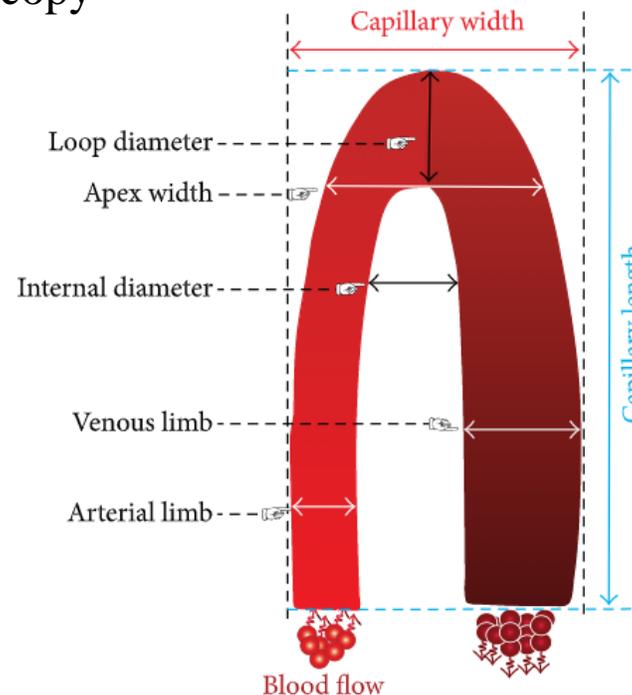
- Water content in tissues is mainly regulated via **transcapillary system**, which compose of small blood capillaries
- Parameters of shallow blood capillaries, such as nailfold capillaries, can be assessed using **optical microscopy (capillaroscopy)**

Parameters usually analyzed in capillaroscopy:

- number of capillaries
- morphology of capillaries:
  - Apical diameter (Loop diameter)
  - Venous limb
  - Arterial limb
- capillary blood flow velocity

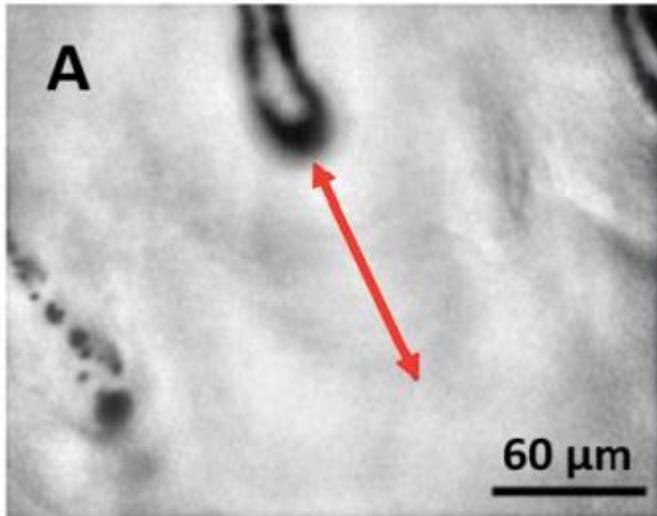
**The main question: Are there any parameters of blood capillaries which are correlated with fluid retention (edema syndrome)?**

Images of capillaries are obtained by capillaroscopy

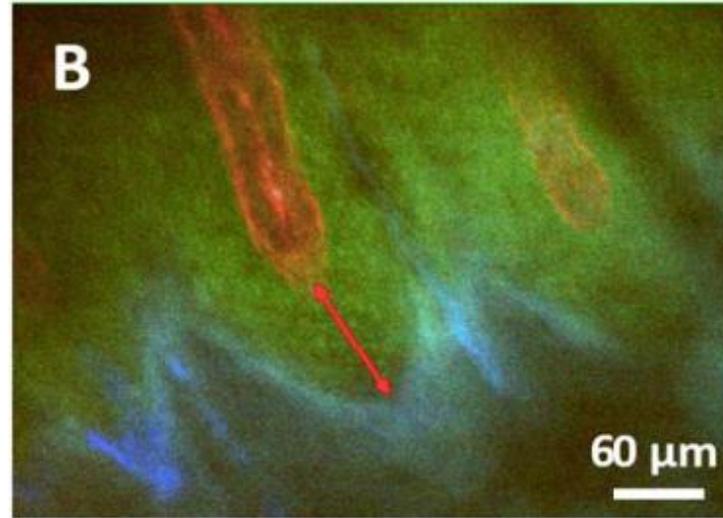


# The size of perivascular zone as the marker of fluid retention

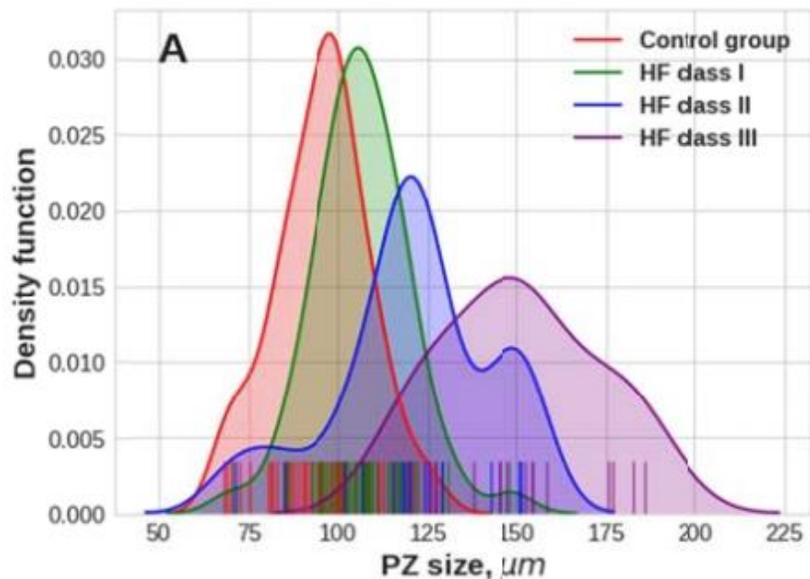
nailfold video capillaroscopy



two photon imaging



- Previously it was demonstrated that edema caused by heart failure can be assessed using the width of the perivascular zone (PZ) – the width of viable epidermis near capillary papillae [1]
- The results of in vivo two-photon tomography of the nailbed capillaries combined with fluorescence lifetime imaging confirm that PZ size is determined by the accumulation of interstitial fluid in the epidermis.



PZ size and shape correlate with

- Arterial hypertension
- Severity of Heart Failure (HF)

[1] Shirshin E.A., et al. Journal of biophotonics (2018): e201800066.

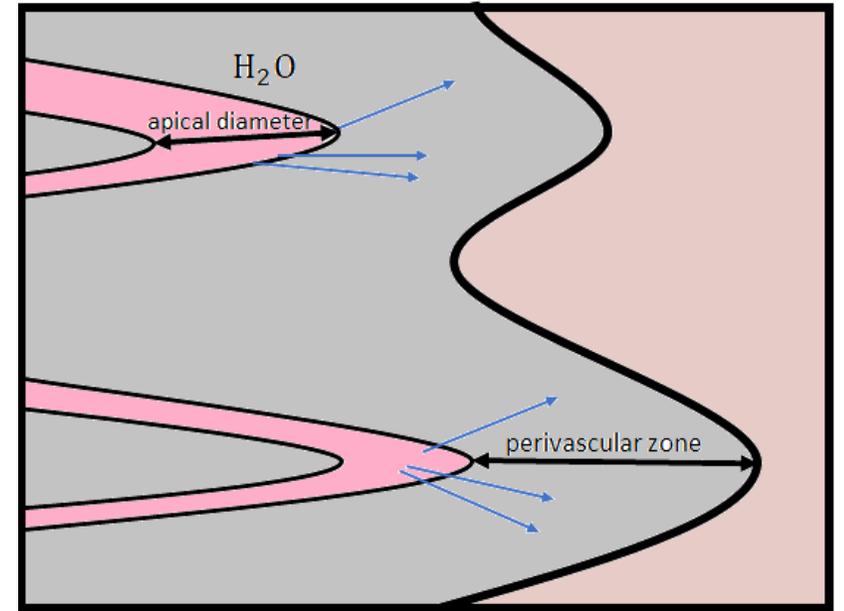
# Aim and Methods

Here we aimed at elucidating specific morphological parameters of shallow blood capillaries which can be easily assessed using optical microscopy and can be used to diagnose the edema syndrome and monitor fluid retention in tissues

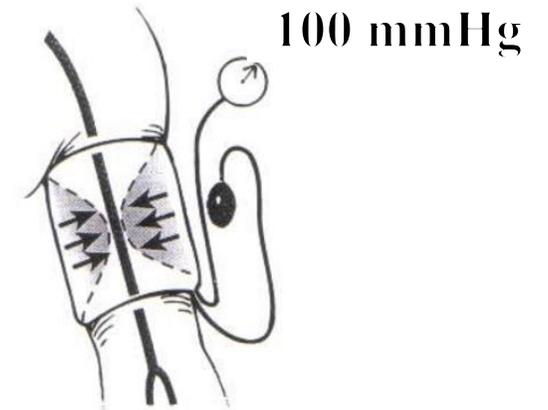
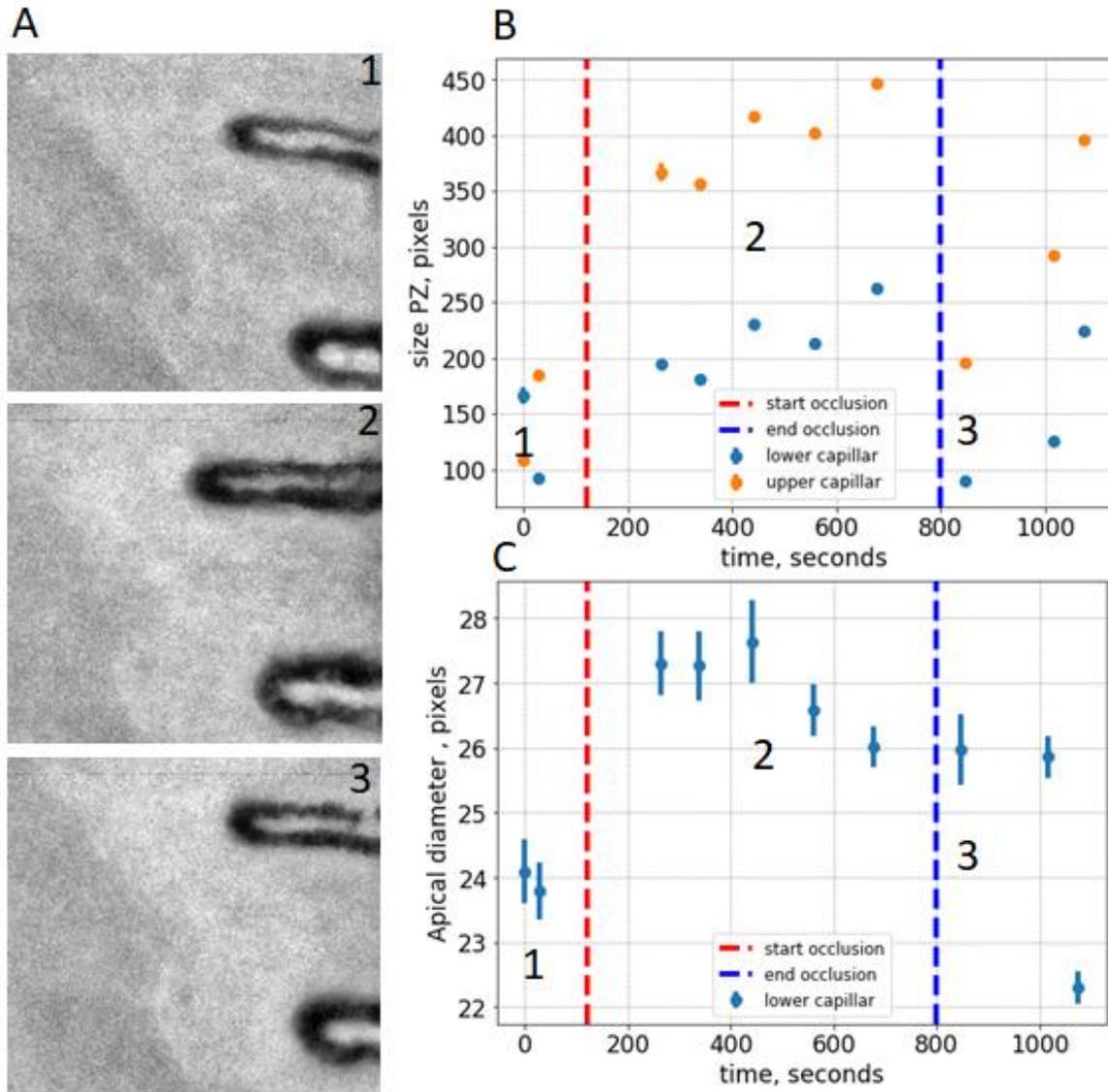
We hypothesize that the size of the **apical diameters** of capillaries and **perivascular zone** should positively correlate with the capillary diameter, since the liquid release in tissues is associated with an increased pressure inside the capillary and should lead to increase of these parameters

To check it, we:

- modeled venous occlusion in vivo using forearm cuff
- evaluated these parameters on volunteers with different severity class of chronic heart failure
- Evaluated these parameters on the cohort of volunteers uptaking diuretics



# Assessment of capillaries parameters during venous occlusion



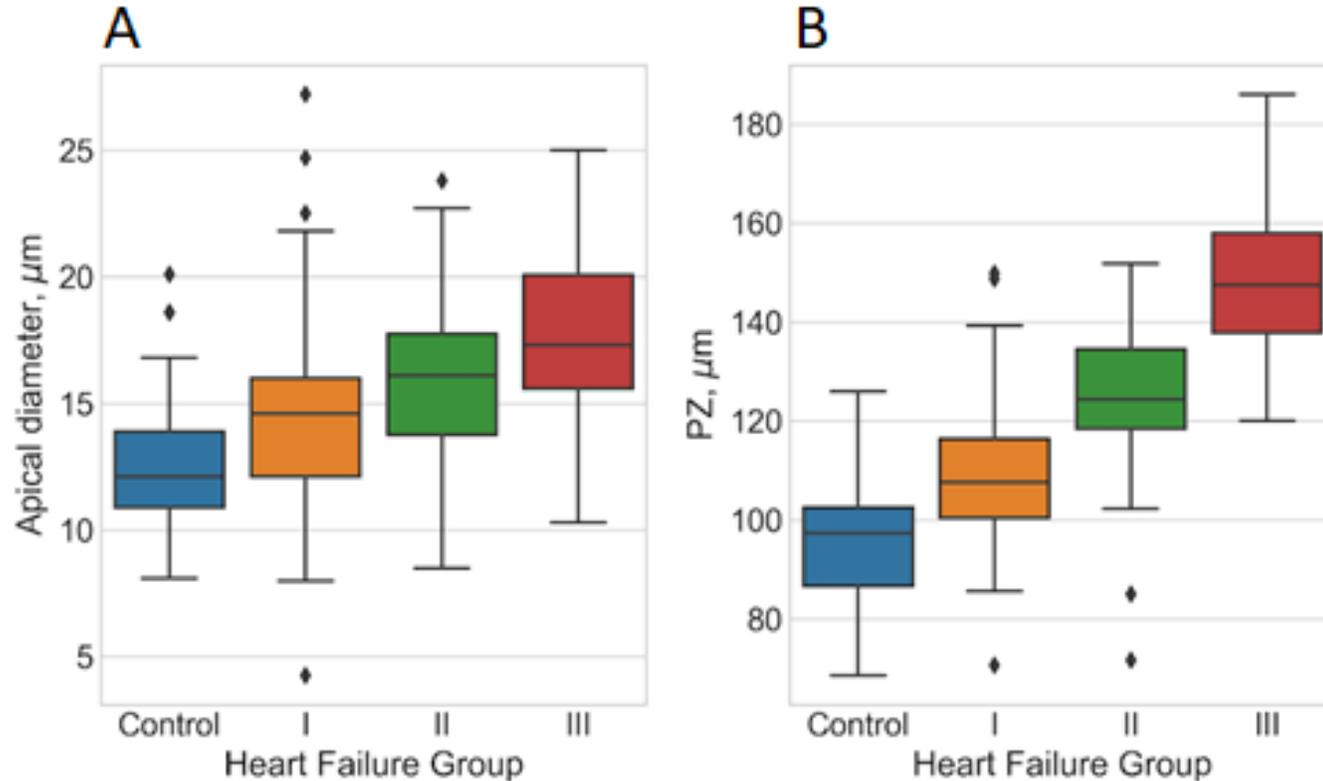
## Measurement protocol:

- Images of capillaries was measured before, during and after occlusion.
- Occlusion parameters: 100 mmHg, 10 minutes

## Results:

- Increase in the width of the perivascular zone by 50% during the first 3 minutes after clamping the forearm.
- With an occlusion duration of more than 3 minutes, the width of the perivascular zone changes slightly.

# Morphological parameters of capillaries and heart failure



## Results:

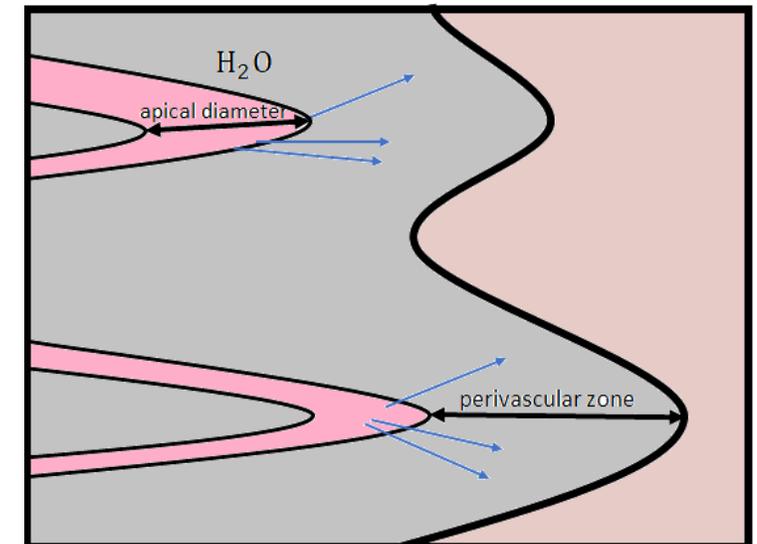
**(A) Apical diameter correlates with the severity of HF**

**(B) PZ correlates with the severity of HF**

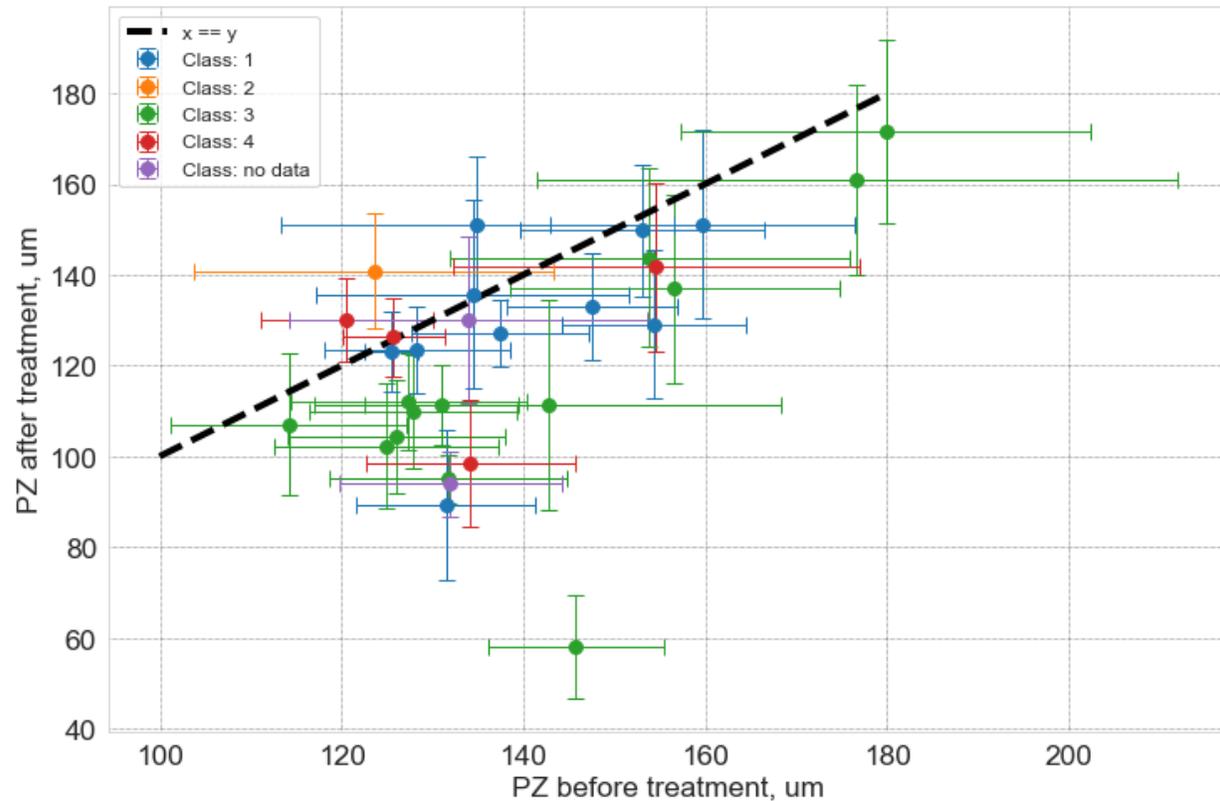
Measurement protocol:

The size of the perivascular zone (PZ) was measured on 129 adult volunteers:

- 79 patients suffering from HF classes I–III according to the NYHA classification.
- 50 healthy volunteers without clinical symptoms of cardiovascular disease



# PZ measurement in patients with CHF after diuretic therapy



## Measurement protocol:

- 64 adult volunteers:
  - 1 - took diuretics
  - 2 – didn't follow the instructions of the doctor
  - 3 - infusions were additionally prescribed
  - 4 – carefully followed the instructions of the doctor
- The size of the perivascular zone (PZ) was measured before and after inpatient therapy.

## Results:

- there is a trend towards a decrease in the size of the PZ as a result of treatment.
- the changes were no more than 20% and were comparable to the standard deviation calculated from measurements of at least five capillaries.

# Conclusions

- Two blood capillary's parameters, namely, perivascular zone and apical diameter, can be assessed using standard wide-field optical microscopy
- These parameters serves as an indicators of fluid retention and may be used for the non-invasive assessment of transcapillary diffusion
- Apical diameter and size of perivascular zone correlate with the severity of heart failure and might be used for pathology diagnostics in a clinical setting.

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