Clinical research with the **rtx1™** Adaptive Optics Retinal Camera

Summary of published results in **Arterial Hypertension**

As cardiovascular events (CVE) are the leading cause of death worldwide, their prevention is of key importance to global health. The most important known risk factor for CVE is arterial hypertension (AHT)[1].

Previous studies demonstrated that analyzing the wall morphology of small arteries could enhance the prediction of CVE[2-6]. Unfortunately, the assessment method required biopsies of subcutaneous arterioles. The invasive nature of this technique has prevented further application in clinical routine[7].

Clinical studies using the rtx1 have resulted in several new findings:

- The rtx1 has enabled direct non-invasive visualization of retinal arteriolar walls[6,8,9]

- It has allowed assessing retinal microvascular biomarkers* with micrometer reproducibility, including lumen diameter (LD) and wall-to-lumen ratio (WLR)[10]

- AHT patients were found to have significantly lower retinal LD and higher WLR when compared with normotensive subjects[8-12]. Such abnormalities were also detected in patients with masked AHT[11]

- Clinical retinal findings with the rtx1 were found to be strongly correlated with ex-vivo measurements in subcutaneous arterioles[10], which are known to provide highly predictive prognostic biomarkers for CVEs[2-6]

- The rtx1 has revealed morphological changes in small arteries during the course of anti-hypertensive therapies, including drug treatments[12] and baroreceptor stimulation[13]

> *The evaluation of microvascular structure is progressively moving from bench to bedside, and it could represent, in the near future, an evaluation to be performed in all hypertensive patients*
>
> Agabiti-Rosei, *Journal of Hypertension*, 2017

> *There is undoubtedly a need for noninvasive approaches in the evaluation of microvascular morphology that may provide us with a better risk stratification of patients, as well as with further important information about the effects of antihypertensive drugs*
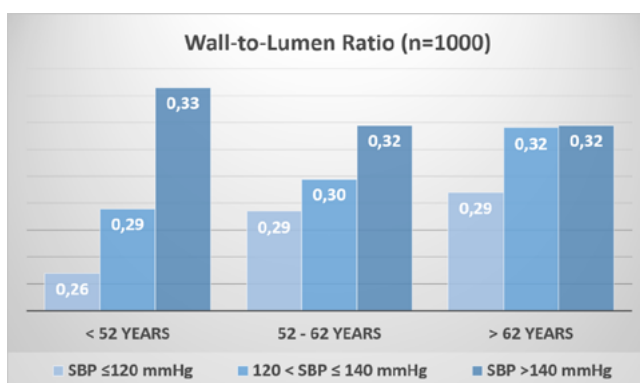>
> Rizzoni & Docchio, *Journal of Hypertension*, 2016

100µm
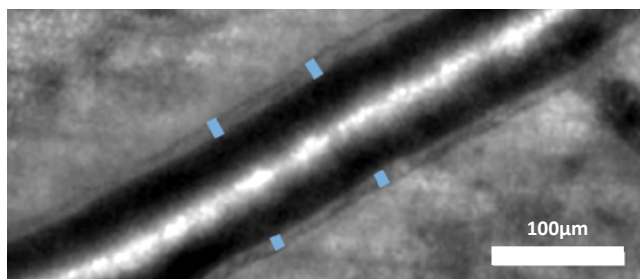
Walls of the retinal arteriole (blue marks) imaged with the rtx1.

> *High resolution imaging of retinal vessels by adaptive optics allows quantitative microvascular phenotyping*
>
> Koch et al. *Journal of Hypertension*, 2014

Wall-to-lumen ratio (WLR) of retinal arterioles vs. blood pressure.
Credit: Rosenbaum et al. 2016

> *Subjects with reported arterial hypertension showed a significantly increased age-adjusted wall-to-lumen ratio*
>
> Meixner et al. *Graefe's Arch. for Clin. and Exp. Ophthalmology* 2015

> ❝ *Noninvasive and easily repeatable procedure such as the evaluation of the arterioles in the fundus oculi by adaptive optics may provide similar information regarding microvascular morphology compared with an invasive, accurate and prognostically relevant micromyographic measurement of the MLR of subcutaneous small arteries*
>
> De Ciuceis et al. *Journal of Hypertension*, 2018

> ❝ *In arterial hypertension, WLR is a robust, dimensionless parameter that can be measured on large cohorts of nondilated patients*
>
> Paques et al. *Prog. in Ret. and Eye Res.*, 2018

Baseline — Focal narrowing WLR = 0.33

After 5 weeks of treatment — Regular caliber WLR = 0.25 — 100µm
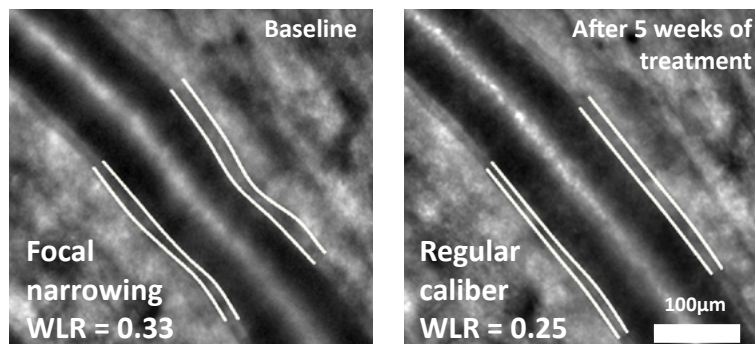
Arteriolar remodeling during anti-hypertensive therapy. Credit: Pitié-Salpétrière Hospital, Paris, France

> ❝ *We were able to observe a decrease in WLR in case of a significant blood pressure drop [...] shortly after antihypertensive treatment introduction or reinforcement*
>
> Rosenbaum et al. *Journal of Hypertension*, 2016

References

1. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment. *The Lancet Diabetes & Endocrinology* 2, 634–647 (2014).

2. Rizzoni, D. et al. Prognostic Significance of Small-Artery Structure in Hypertension. *Circulation* 108, 2230–2235 (2003).

3. Mathiassen, O. N. et al. Small artery structure is an independent predictor of cardiovascular events in essential hypertension. *Journal of Hypertension* 25, 1021–1026 (2007).

4. De Ciuceis, C. et al. Structural Alterations of Subcutaneous Small-Resistance Arteries May Predict Major Cardiovascular Events in Patients With Hypertension. *American Journal of Hypertension* 20, 846–852 (2007).

5. Buus, N. H. et al. Small artery structure during antihypertensive therapy is an independent predictor of cardiovascular events in essential hypertension. *Journal of Hypertension* 31, 791–797 (2013).

6. Agabiti-Rosei, E. & Rizzoni, D. Microvascular Structure as a Prognostically Relevant Endpoint. *Journal of Hypertension* 35, 914–921 (2017).

7. Mancia, G. et al. Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document. *Journal of Hypertension* 27, 2121–2158 (2009).

8. Koch, E. et al. Morphometric Analysis of Small Arteries in the Human Retina Using Adaptive Optics Imaging. *Journal of Hypertension* 32, 890–898 (2014).

9. Meixner, E. & Michelson, G. Measurement of Retinal Wall-to-Lumen Ratio by Adaptive Optics Retinal Camera: A Clinical Research. *Graefe's Archive for Clinical and Experimental Ophthalmology* 253, 1985–1995 (2015).

10. De Ciuceis, C. et al. Comparison Between Invasive and Noninvasive Techniques of Evaluation of Microvascular Structural Alterations. *Journal of Hypertension* 36, 1154–1163 (2018).

11. Gallo, A. et al. Retinal Arteriolar Remodeling Evaluated with Adaptive Optics Camera: Relationship with Blood Pressure Levels. *Annales de Cardiologie et d'Angéiologie* 65, 203–207 (2016).

12. Rosenbaum, D. et al. Effects of Age, Blood Pressure and Antihypertensive Treatments on Retinal Arterioles Remodeling Assessed by Adaptive Optics. *Journal of Hypertension* 34, 1115–1122 (2016).

13. Gallo, A., Rosenbaum, D., Kanagasabapathy, C. & Girerd, X. Effects of Carotid Baroreceptor Stimulation on Retinal Arteriole Remodeling Evaluated with Adaptive Optics Camera in Resistant Hypertensive Patients. *Annales de Cardiologie et d'Angéiologie* 66, 165–170 (2017).

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