

September 12-14

2018

Les Comtes de Méan
Liège, Belgium

6th International Meeting on Aortic Diseases

New insights into an old problem CHU Liège, APF

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Critical review of the murine AAA models

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Disclosure of Interest

Speaker name: Raphaël Coscas

- I have the following potential conflicts of interest to report:
- Consulting: Medtronic, Bard, Abbott, Spectranetics, Terumo
- Employment in industry
- Shareholder in a healthcare company
- Owner of a healthcare company
- Other(s)
- I do not have any potential conflict of interest



Less open surgery and aortic specimens

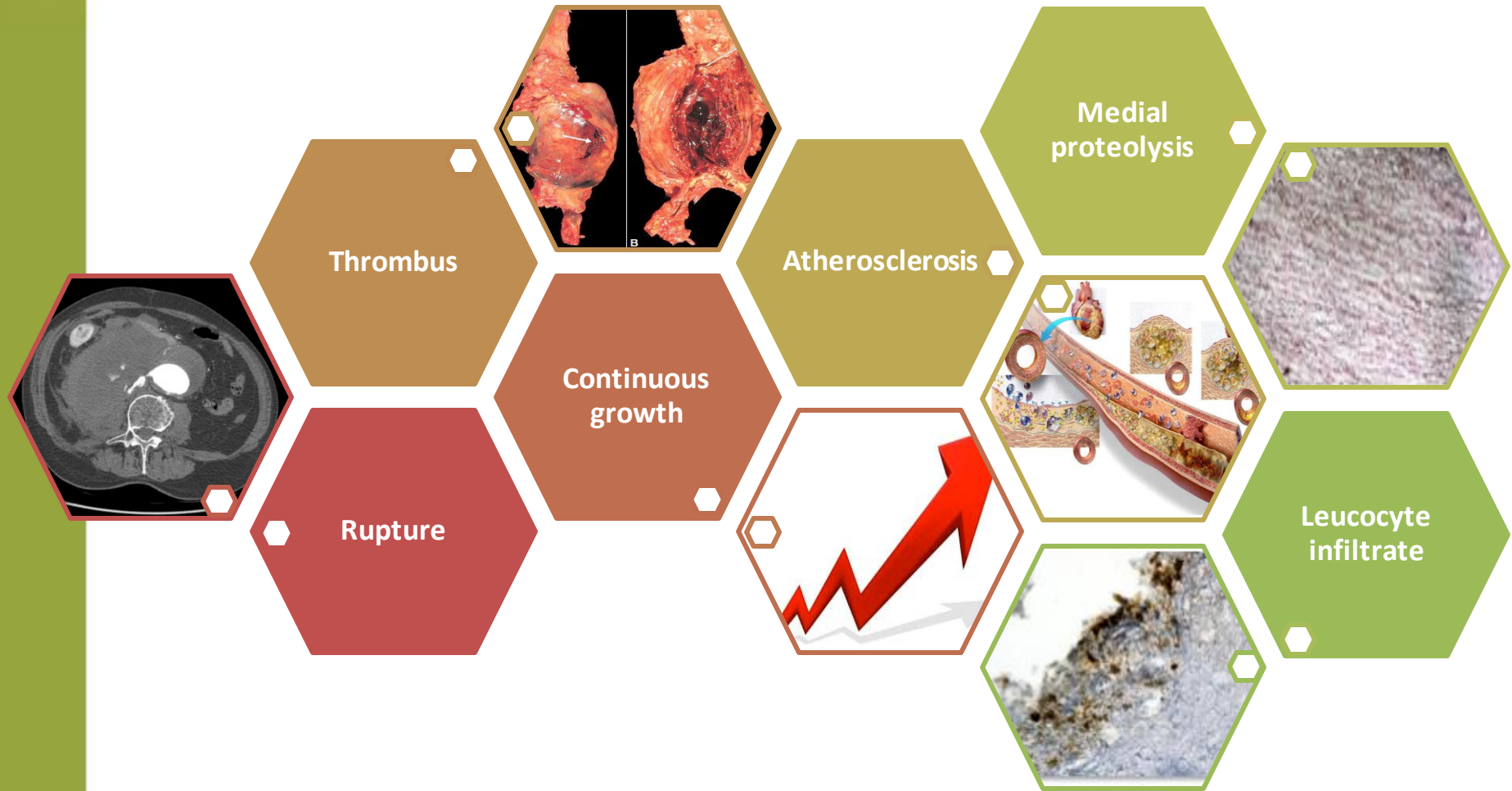
Diagnosis and interventions at late
disease stage

No clearly proven medical therapy



Experimental AAA Models

The ideal AAA model



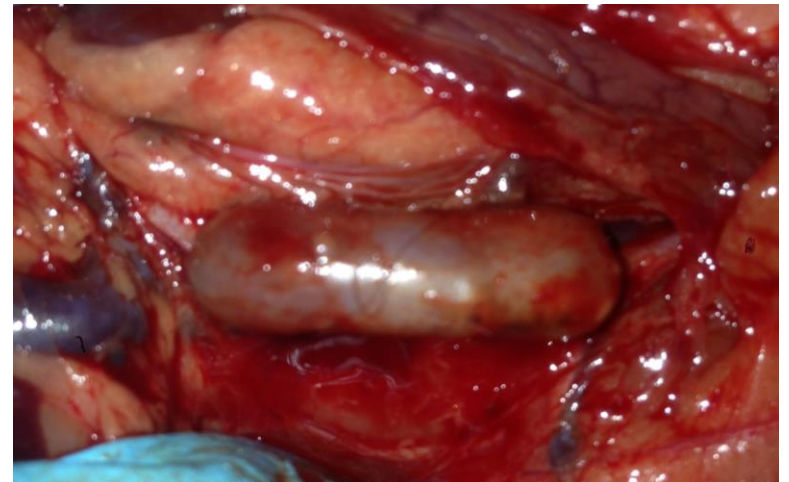
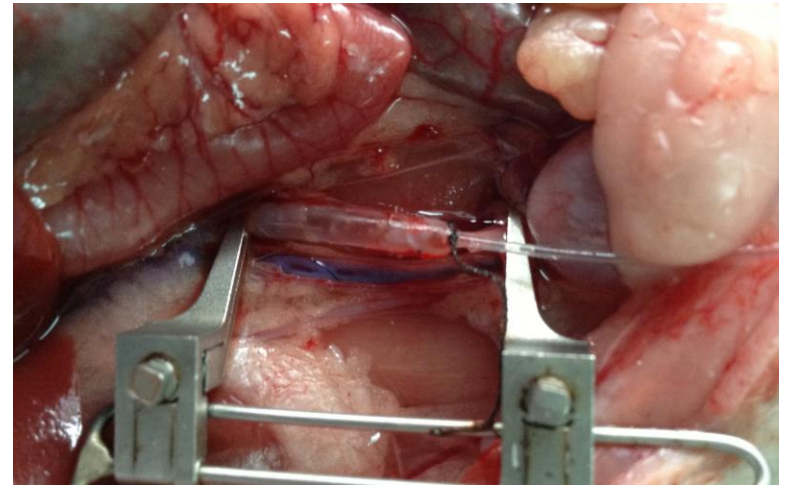
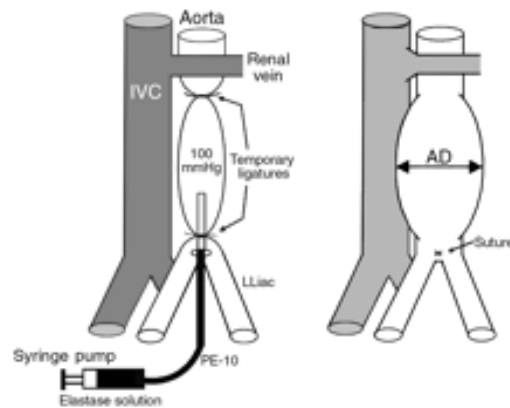
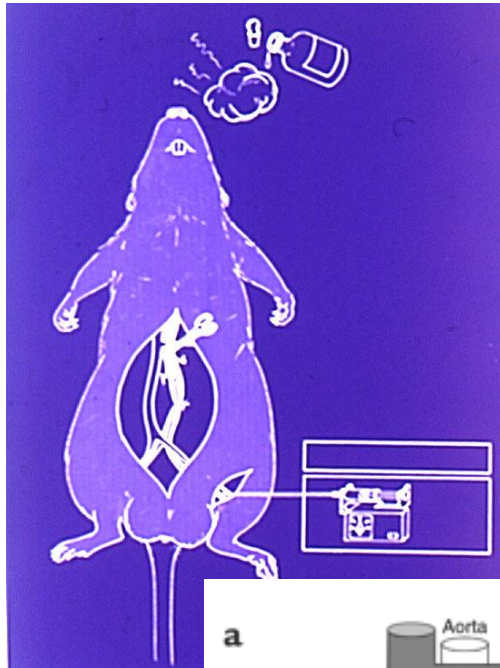


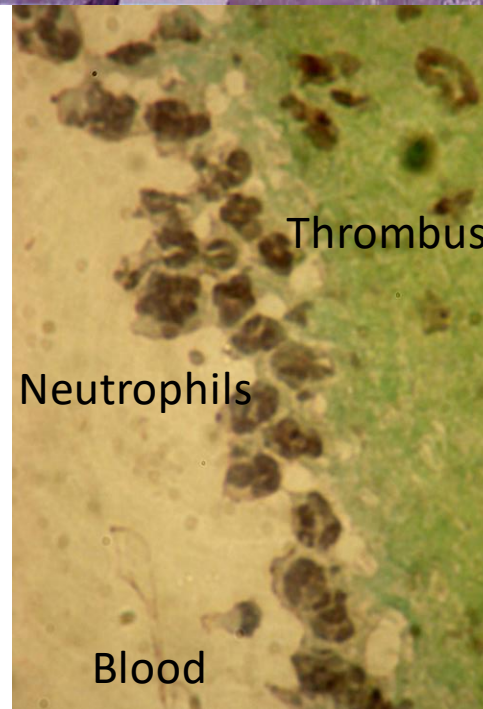
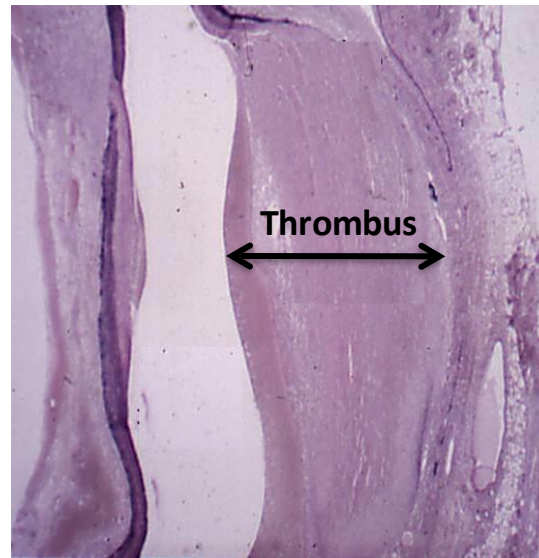
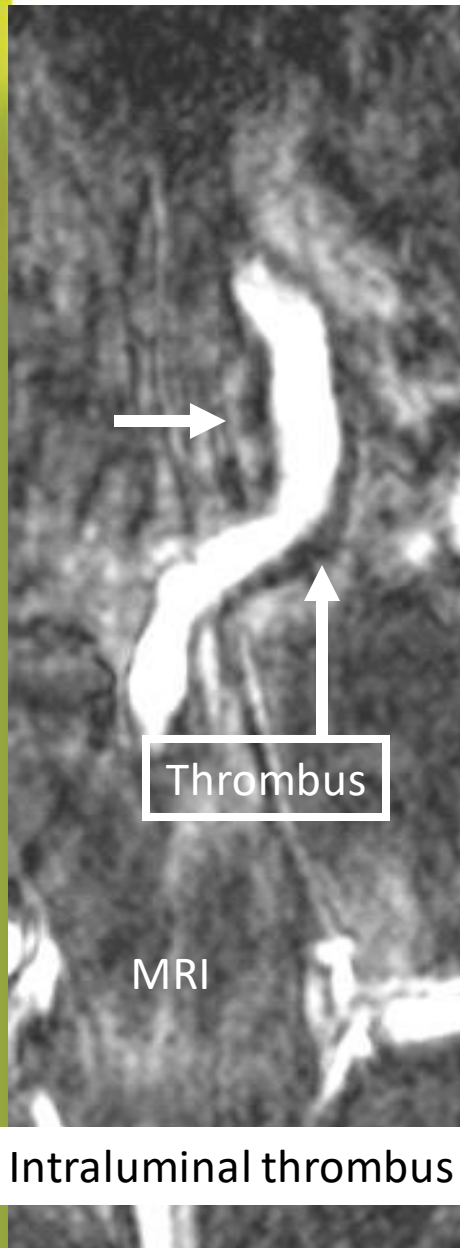
Classifications of current AAA models

- Murine / Large animals
- Surgical / Chemical / Genetic
- Non dissecting / Dissecting



Intra-aortic Elastase Perfusion





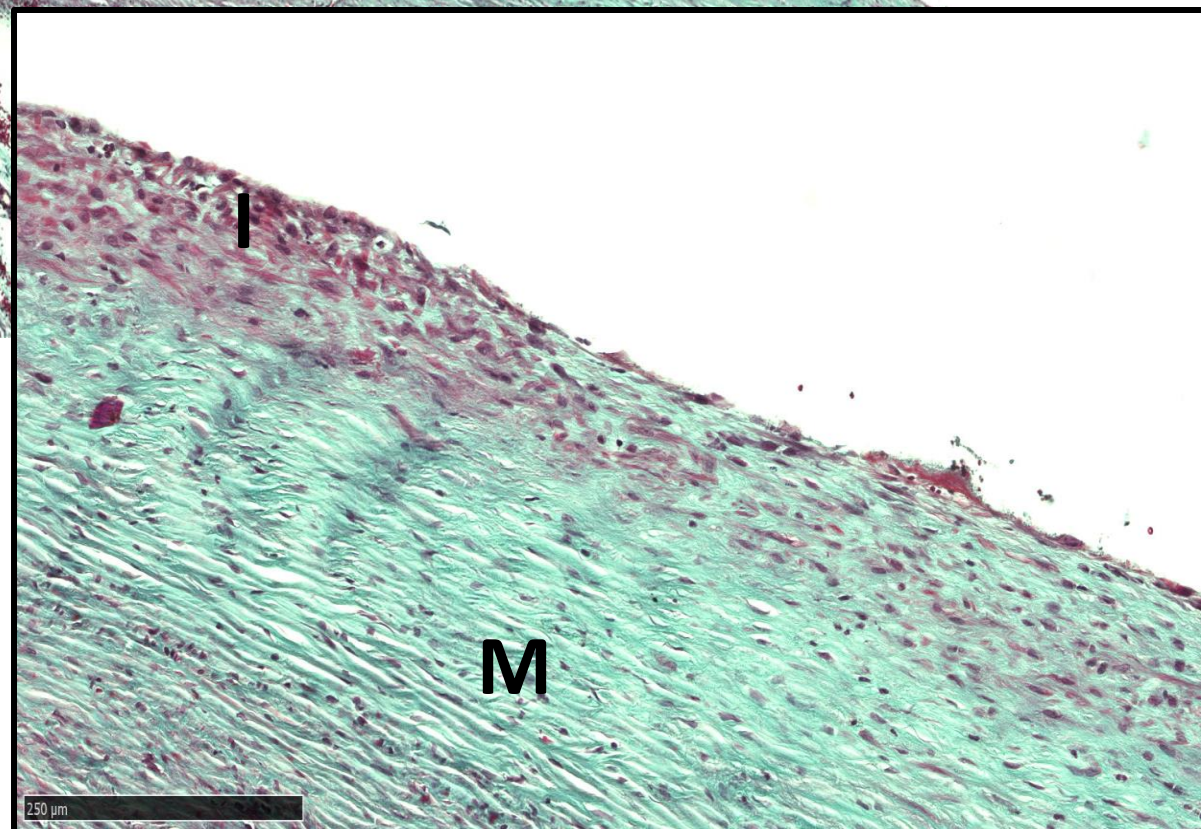
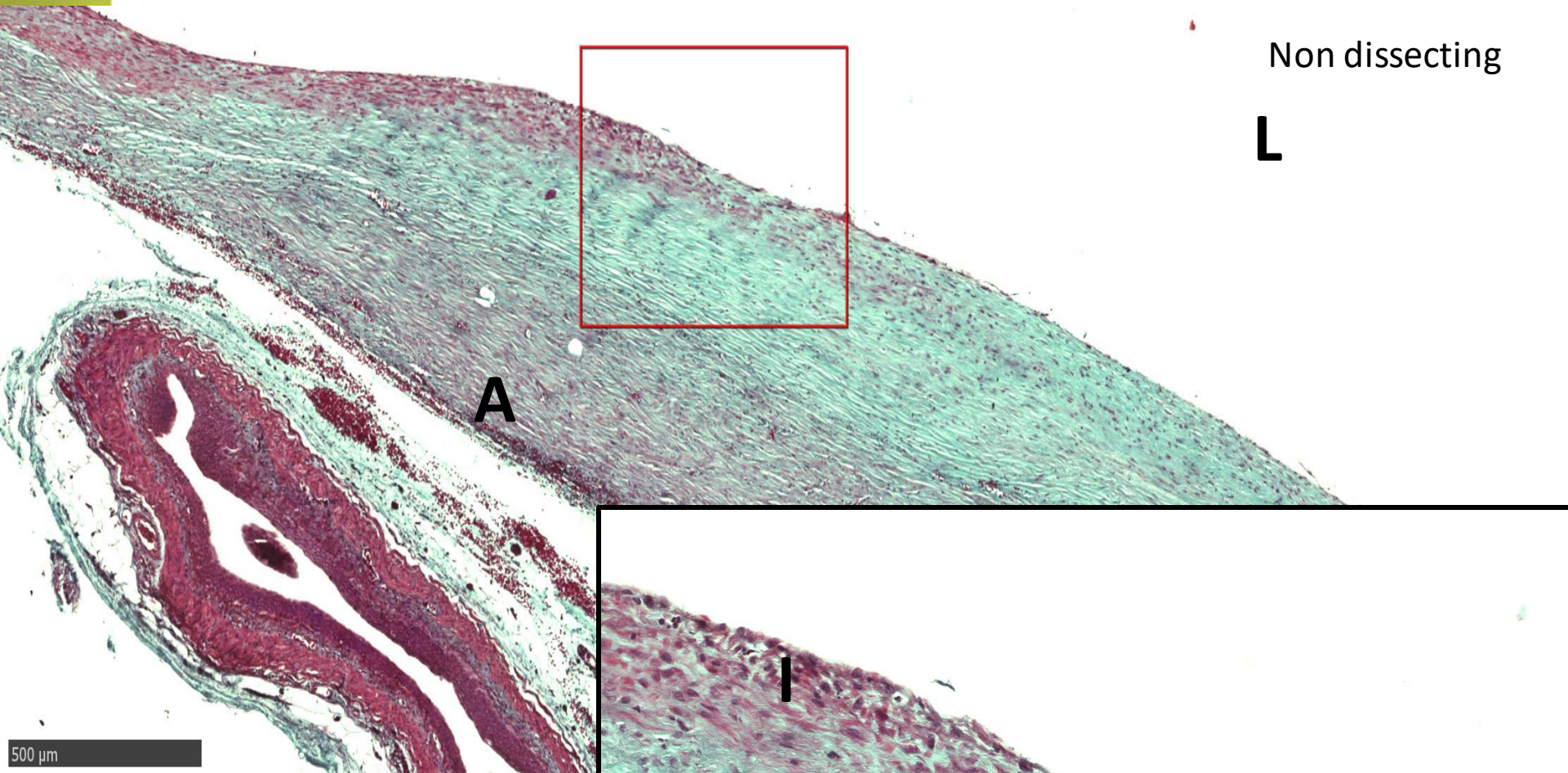
Non dissecting

- Simple
- Thrombus
- ECM destruction

- Not constant
- No rupture
- Healing

- Porphyromonas
Gingivalis
injections

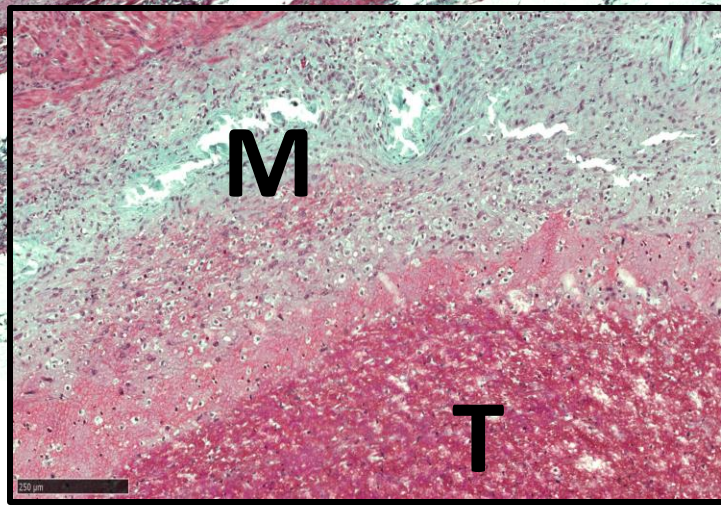
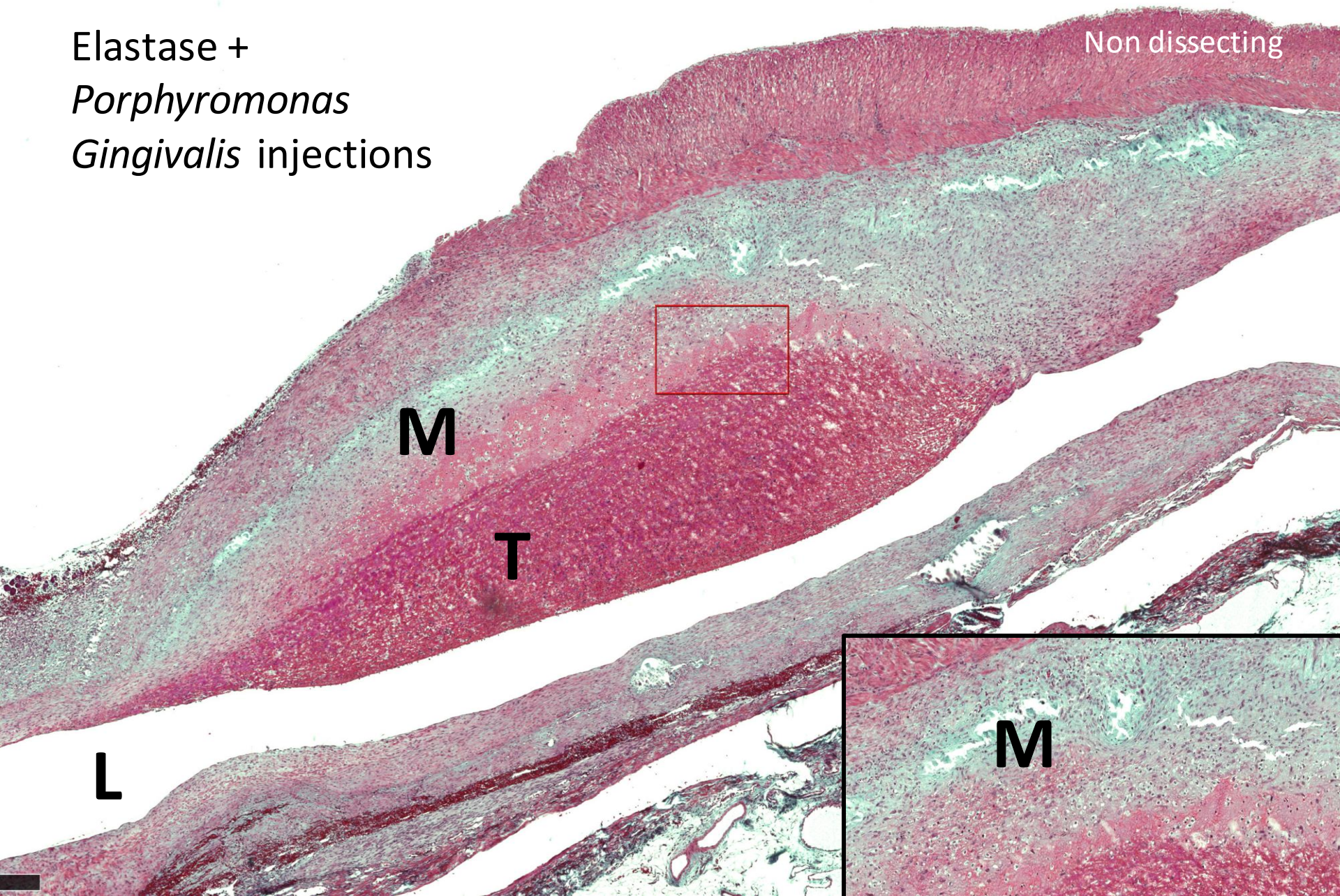
Coutard et al. J Vasc Res 2009
Delbosc et al. J Vasc Surg 2014



Healing at Day 21
Mesenchymal cells

Elastase +
Porphyromonas
Gingivalis injections

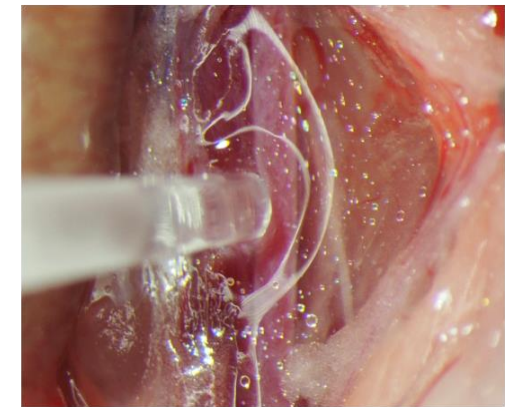
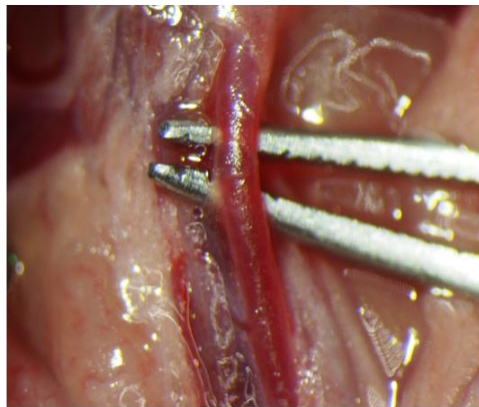
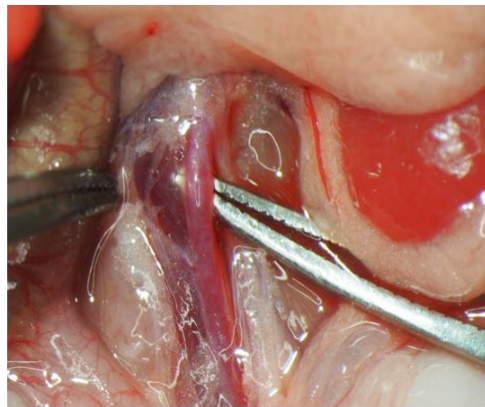
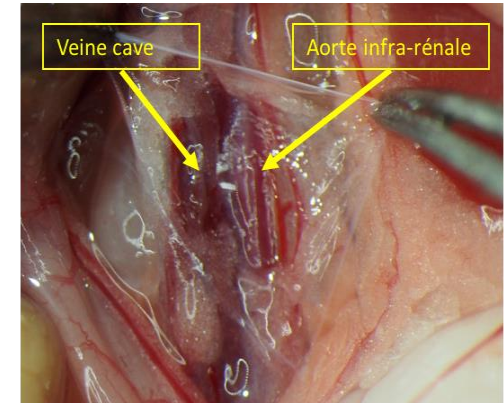
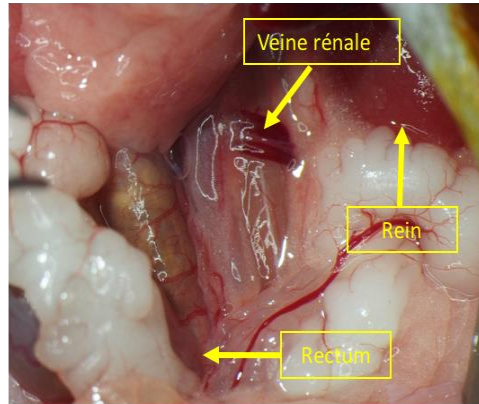
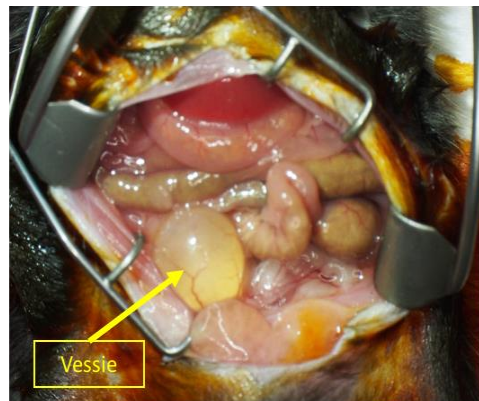
Non dissecting



x10



Adventitial elastase application

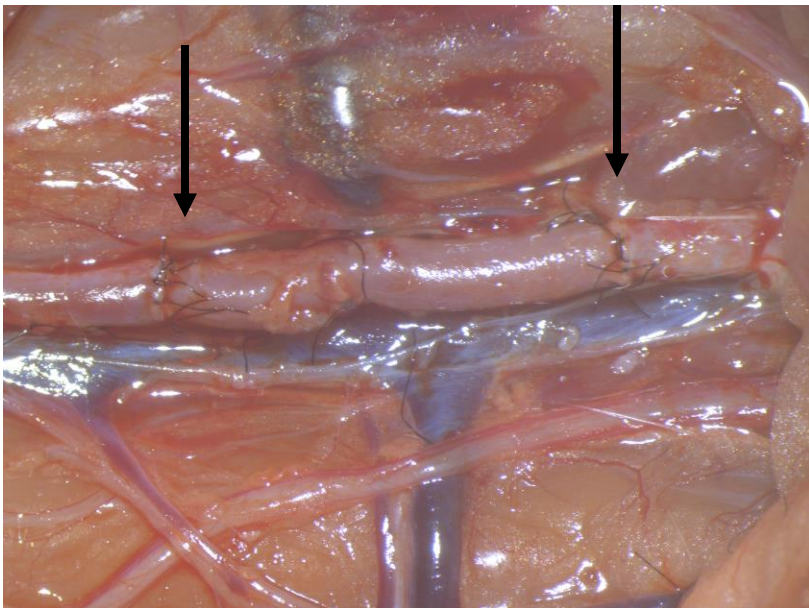


Useful in mice

Genetic modifications

Decellularized aortic xenograft

- Guinea pig → Lewis rat
- Decellularization SDS
- ECM assessment



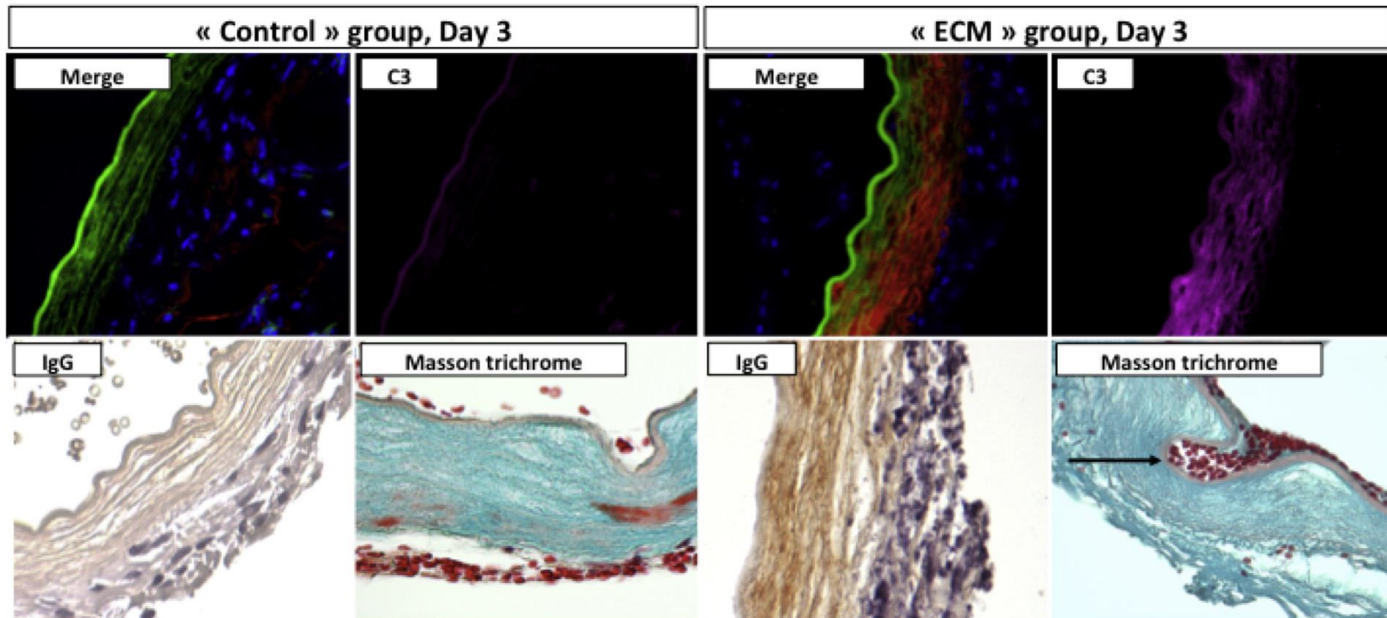
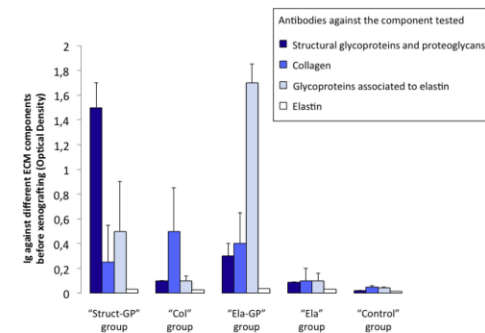
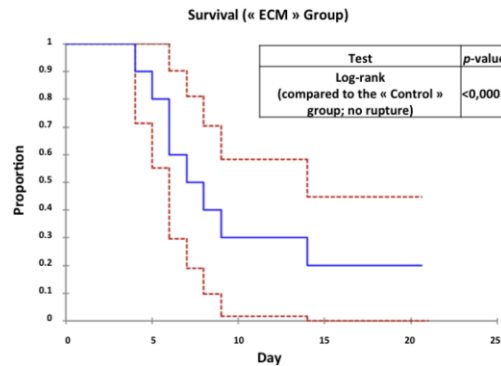
- Constant
- Thrombus
- ECM destruction
- Adaptive immunity

- Micro-surgery
- No rupture
- Healing

- Porphyromonas
Gingivalis injections



Rupture induced through adaptive immunity activation



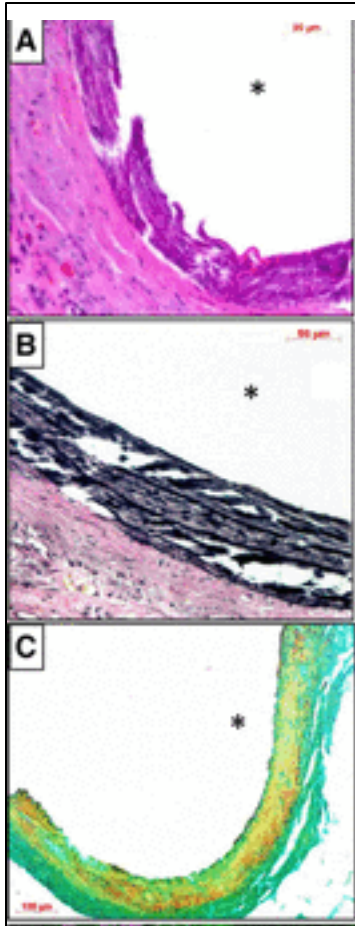
Allaire A et al. *J Clin Invest* 1998
 Coscas R, Michel JB et al. *J Vasc Surg* 2018

Calcium Chloride Application

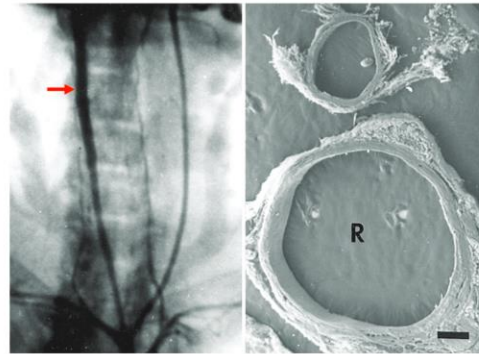
HE

Orcein

Alizarine red



CaCl₂



- Simple
- Mice
- Intercellular Conductance
- Calcifications

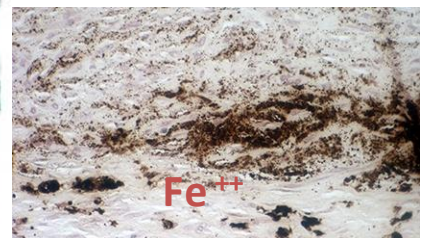
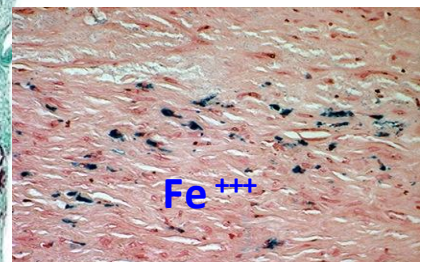
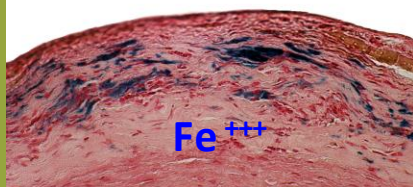
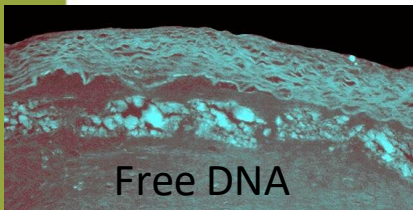
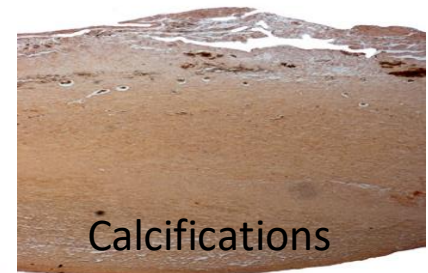
- Moderate dilatation
- No atheroma
- No Thrombus
- No rupture
- Healing

Saccular Aneurysm



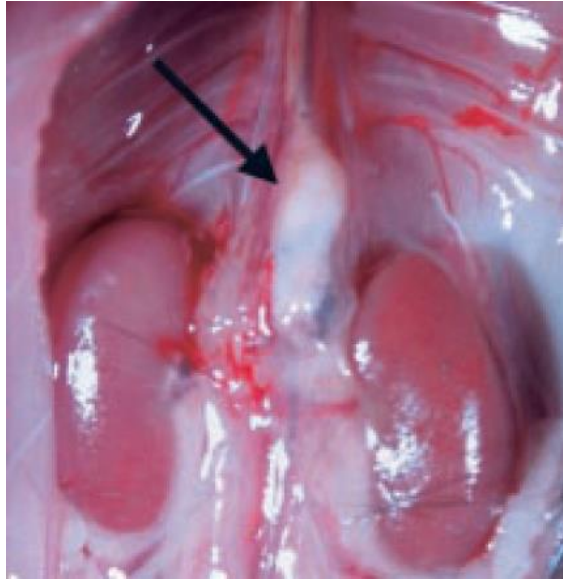
Saccular

Fusiform



H. Etienne, Coscas R, Michel JB et al., presented at the 2017 ESVS congress

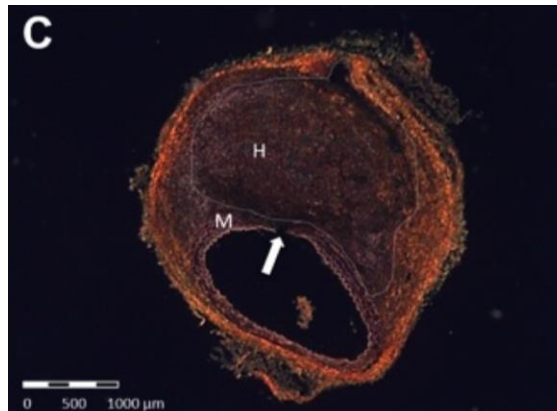
Angiotensin II perfusion + High fat diet



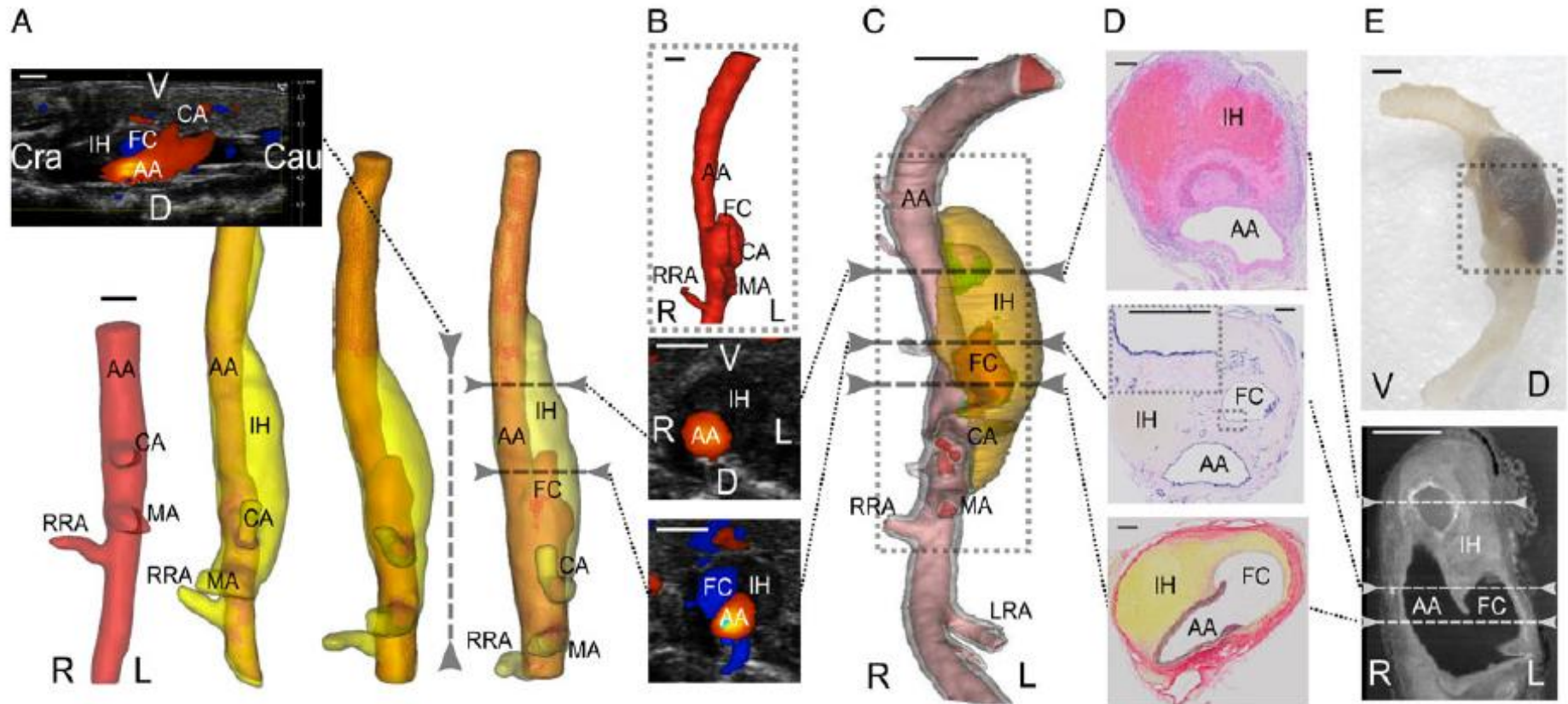
- Apo E -/- Mice
- Dissecting aneurysm

- Simple
- Thrombus

- Not constant
- Suprarenal
- Parietal thrombus
- Healing

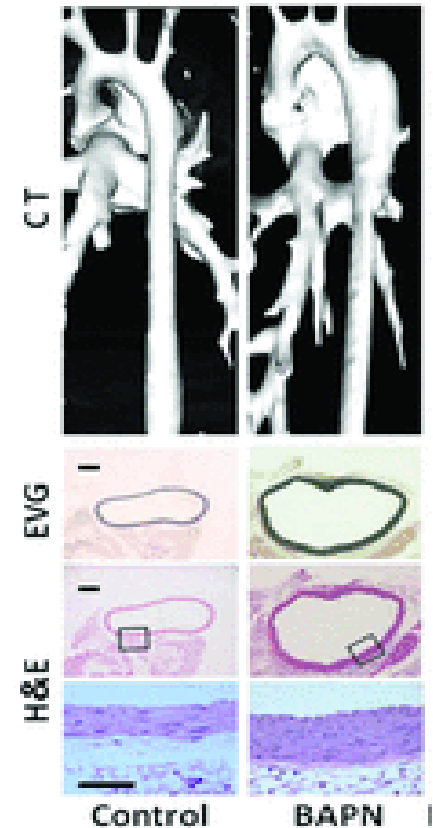


Daugherty et al. J Clin Invest 2000



β -aminopropionitrile administration

- « Lox » inhibitor
- ECM maturation
- Genetic model: « Blotchy Mouse »
- Family thoracic aneurysms
- Association with angiotensin II leads to Rupture



Maki et al. Circulation 2002
Andrews et al. Am J Pathol 1975



AAA models vs. human AAAs

	Human Pathology	Aortic Elastase Perfusion	Xenograft	CaCl ₂ Application	Angiotensin II Perfusion	BAPN	Saccular Model	MCR Agonist + Salt
Rupture	+	—*	—	—	+	+	+†	+
Wall disruption/ dissection	+	—	—	—	+	+	+†	+
Persistent growth	+	—	—	—	—	—	+†	—
ILT	+	+	+	—	—	—	+	—
IMT	+	—	—	—	+	—	—	+
Atherosclerosis	+	—	—	—	+	—	—	—
Medial degeneration	+	+	+	+	+	+	+	+
Leukocyte infiltration	+	+	+	+	+	—	+	+

BAPN indicates β -aminopropionitrile; CaCl₂, calcium chloride; ILT, intraluminal thrombus; IMT, intramural thrombus; and MCR, mineralocorticoid receptor.

*May occur very early.

†Observed when using decellularized grafts

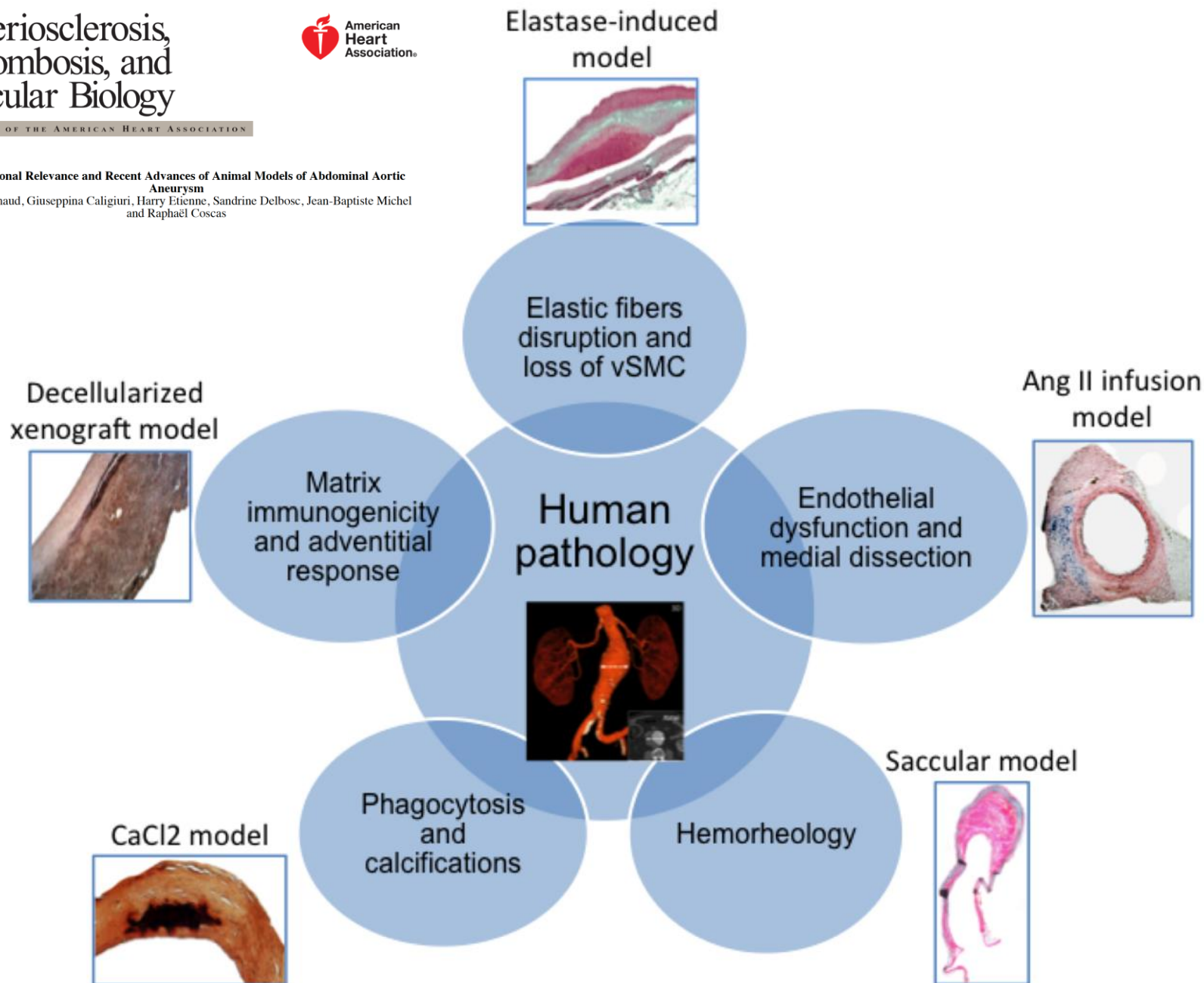


Arteriosclerosis, Thrombosis, and Vascular Biology

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Translational Relevance and Recent Advances of Animal Models of Abdominal Aortic Aneurysm
Jean Sénémaud, Giuseppina Caligiuri, Harry Etienne, Sandrine Delbosc, Jean-Baptiste Michel and Raphaël Coscas



Senemaud J, Michel JB, Coscas R. ATVB 2017



Conclusion

- The ideal AAA model has not been created yet
- Each model allows to study one part of the human pathophysiology
- Research should focus on models with continuous growth and/or rupture

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Thanks



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