

Patho-anatomy and semantic of mitral valve lesions/ dysfunctions : Prolapse, flail, Billowing and annular disjunction (MAD)

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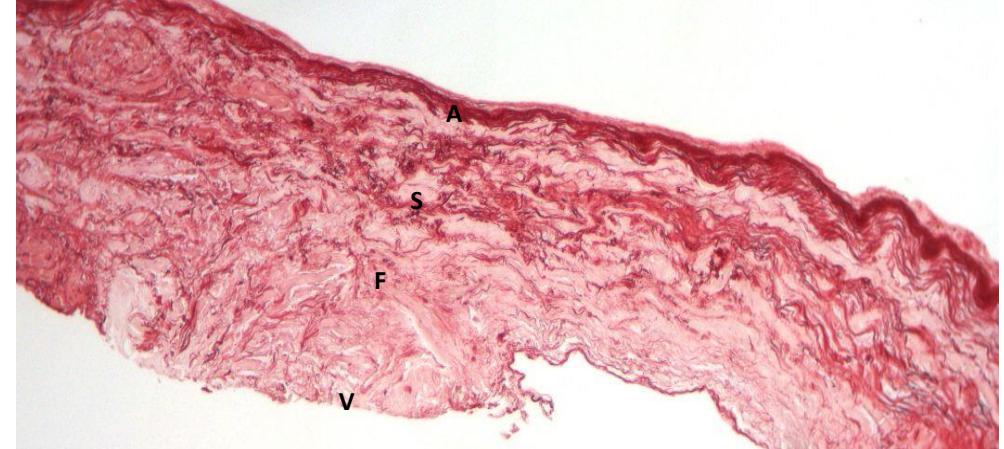
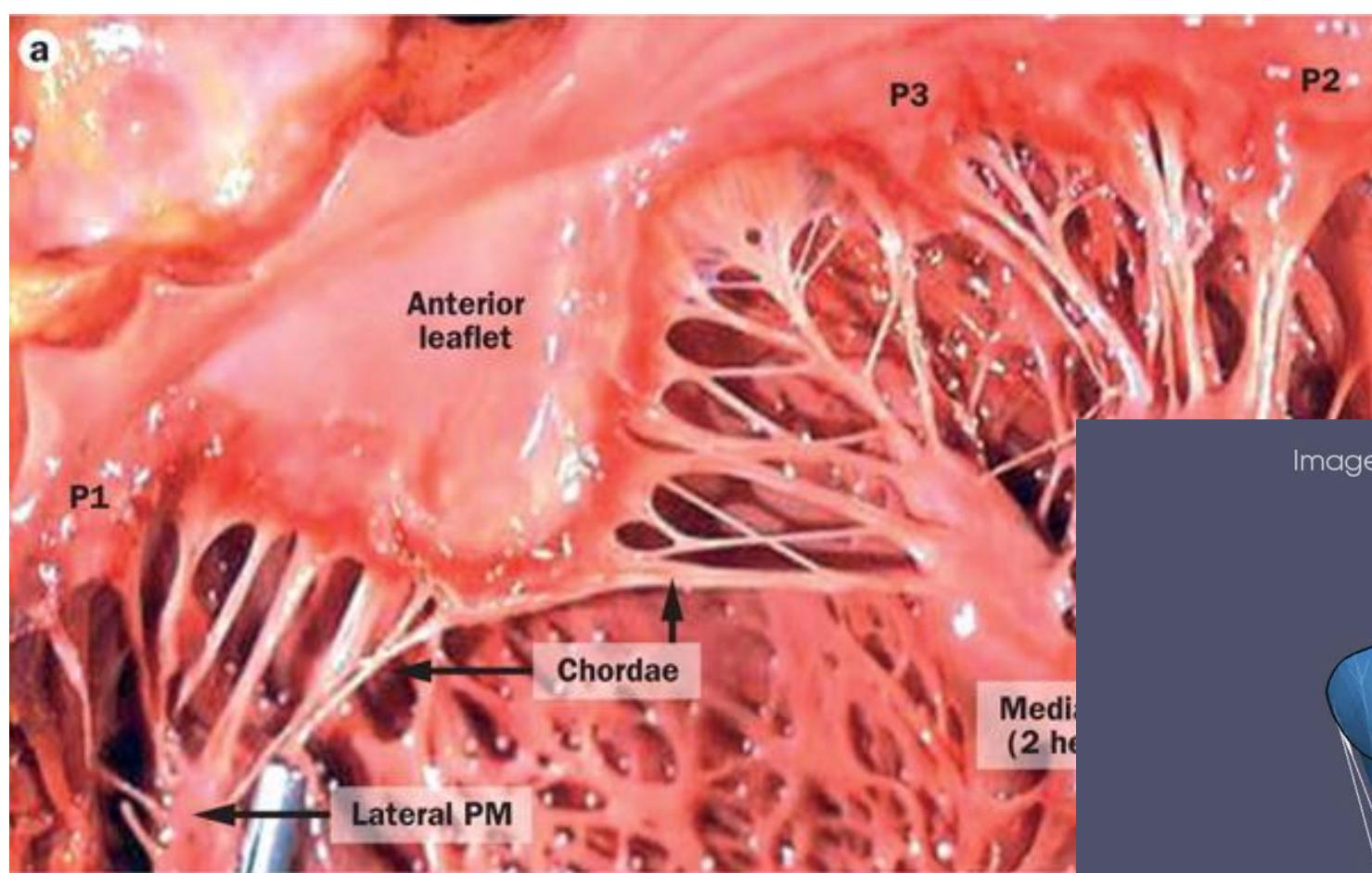
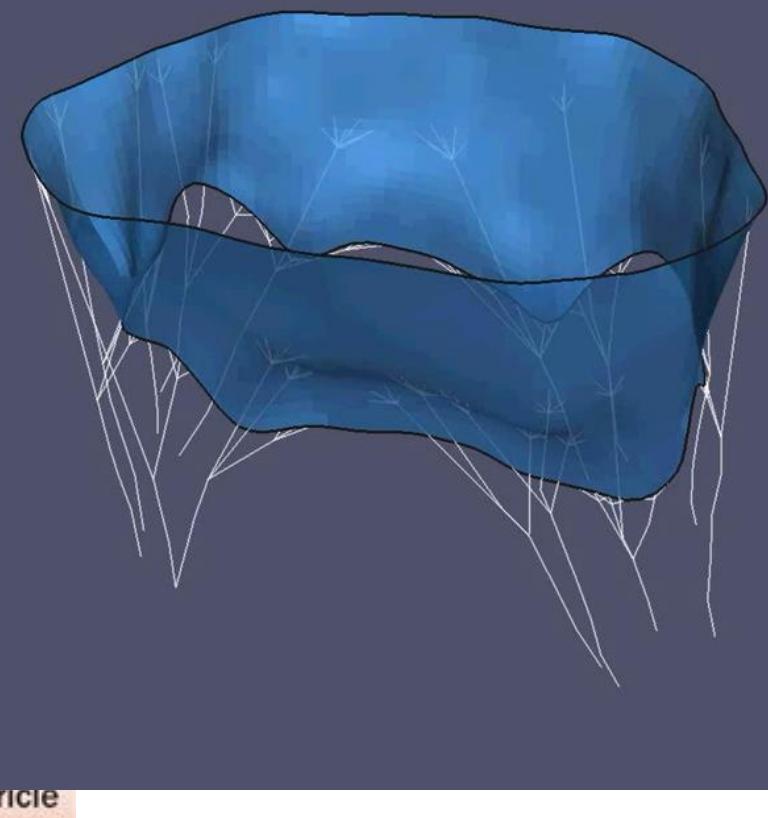
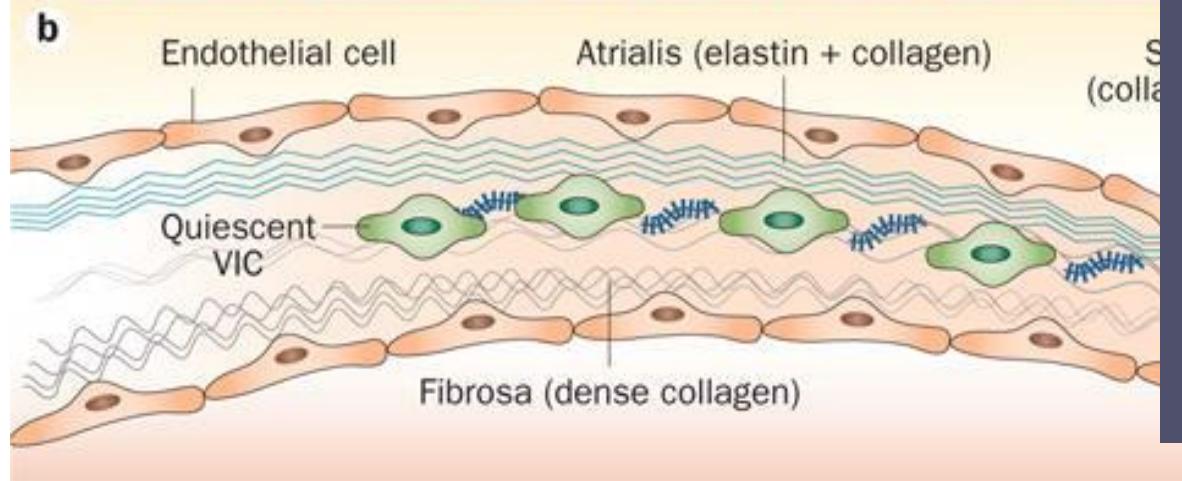


Image-Based Reconstruction of Mitral Valve Finite Element Model



Definition:

- Prolapse ; Chute (ptôse) d'un organe, d'une partie d'organe ou d'un tissu par suite du relâchement de ses moyens de fixation.



billary leaflet

n. ballonnement valvulaire

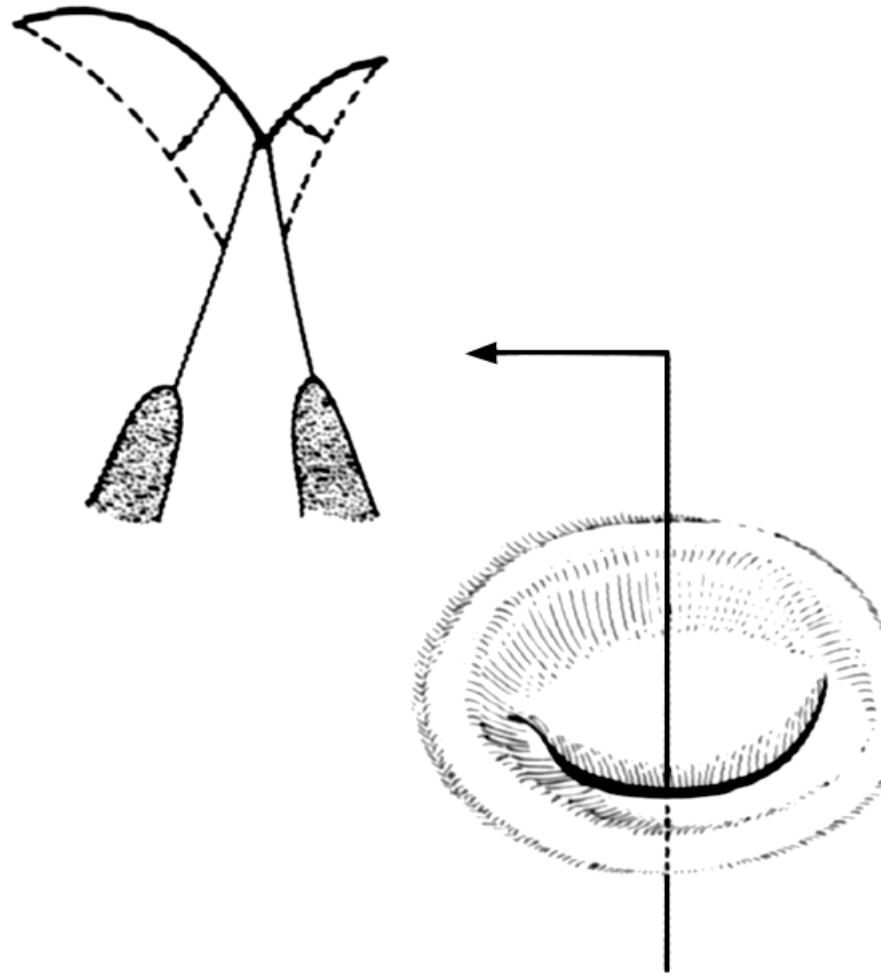
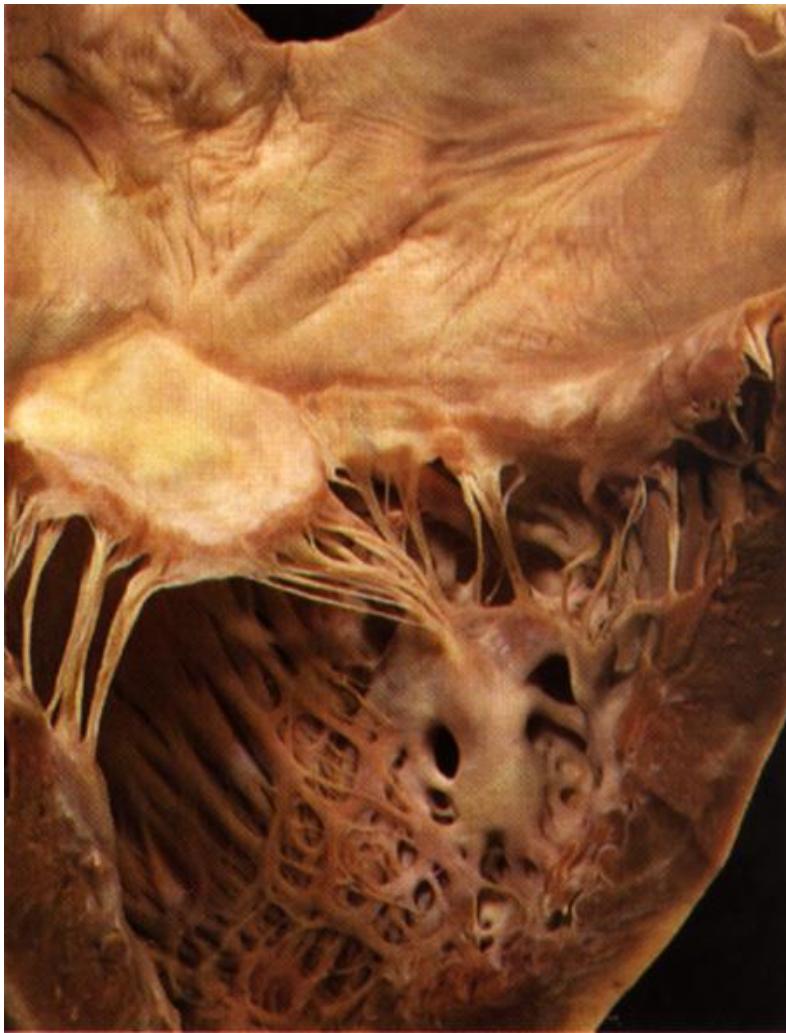
[Med.]

billary mitral leaflet syndrome

n. ballonnement de la valve
mitrale

[Med.]

Functional analysis of Pr A Carpentier



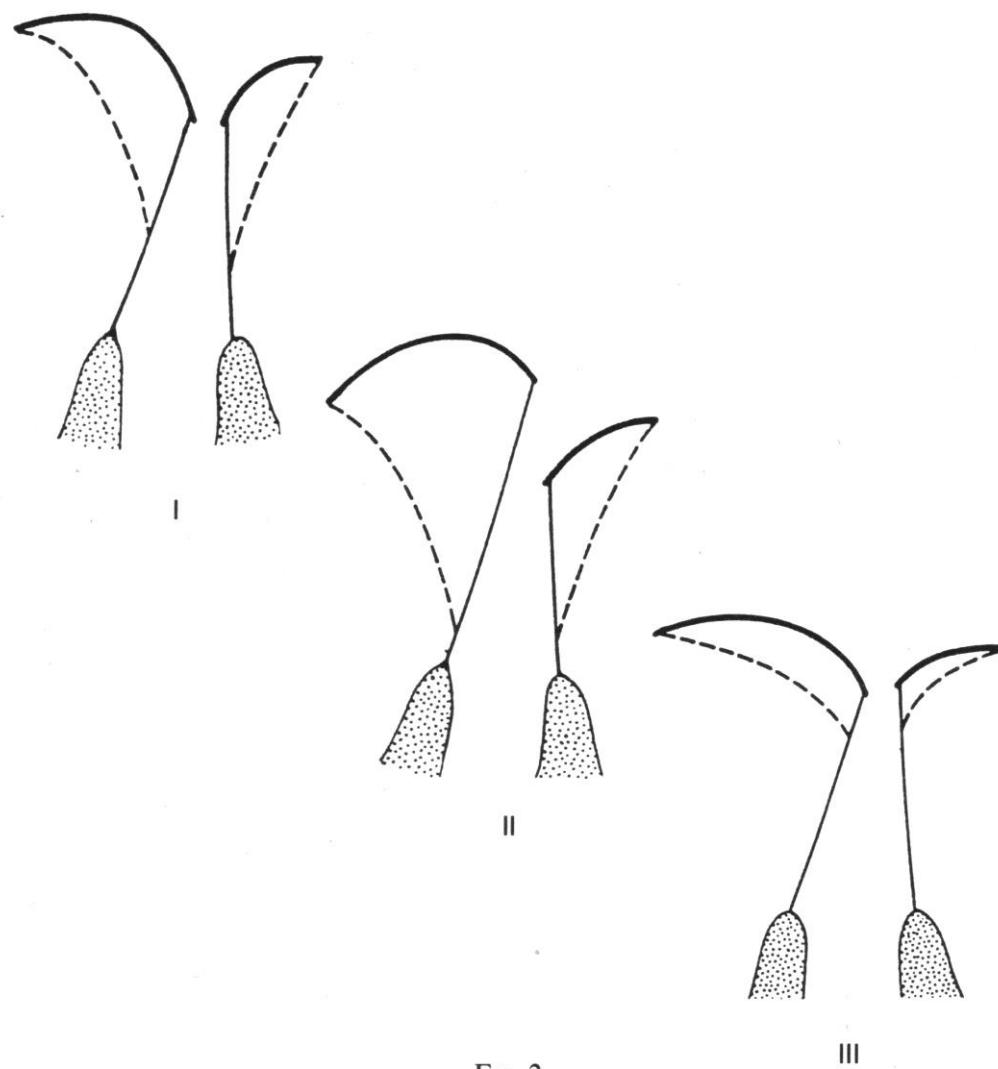
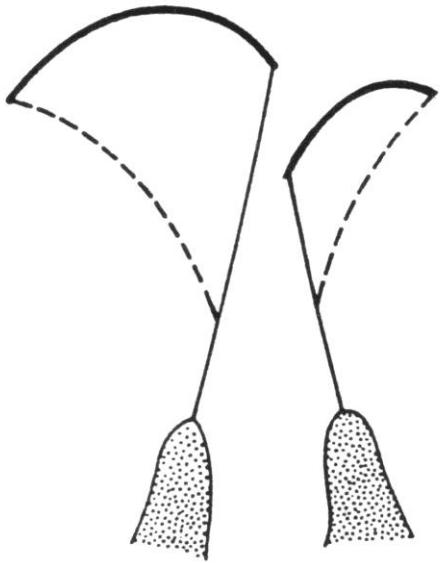


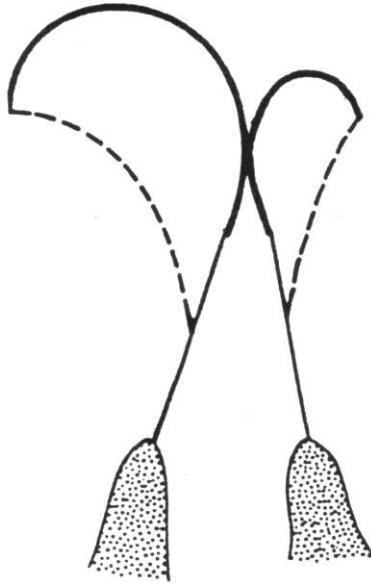
FIG. 2.

On remarquera que le terme « *prolapsus valvulaire* » reprend dans cette classification sa signification originelle. C'est une dysfonction et non une maladie et en particulier nullement une maladie de Barlow.

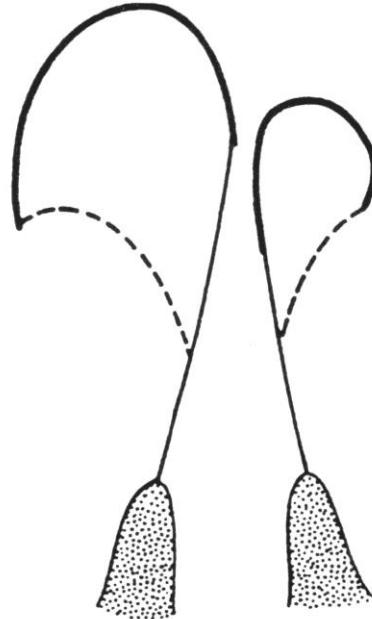
Cette classification appelle deux remarques complémentaires :



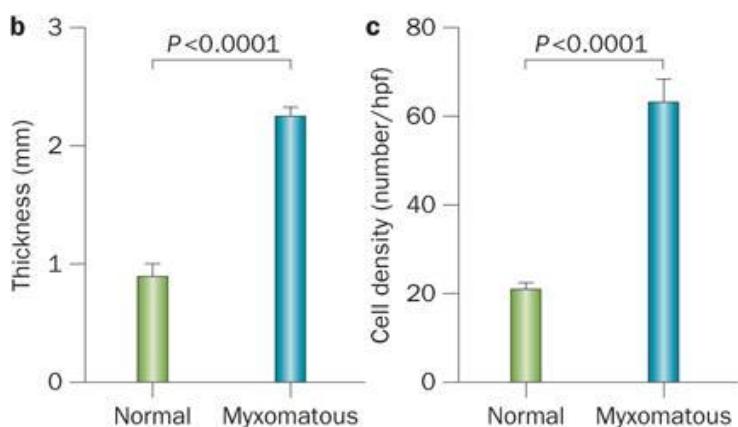
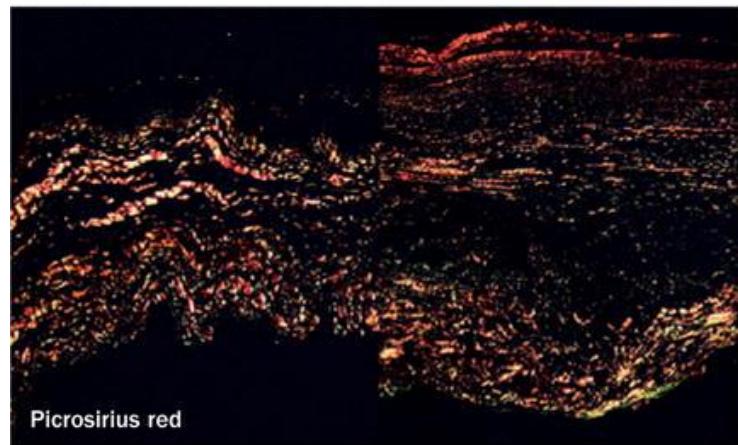
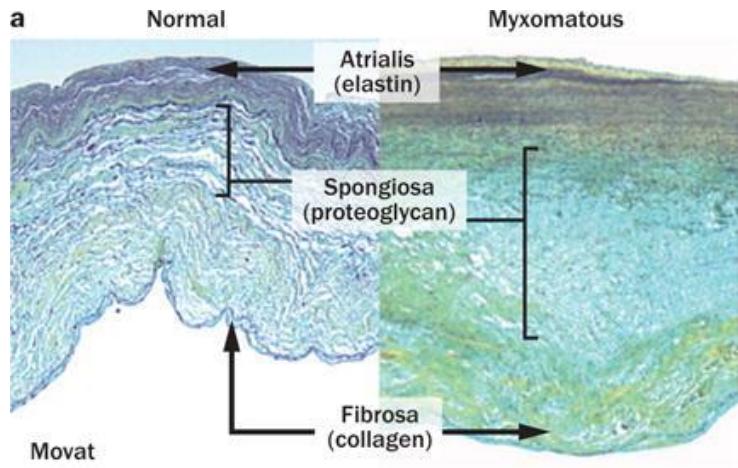
Prolapsus



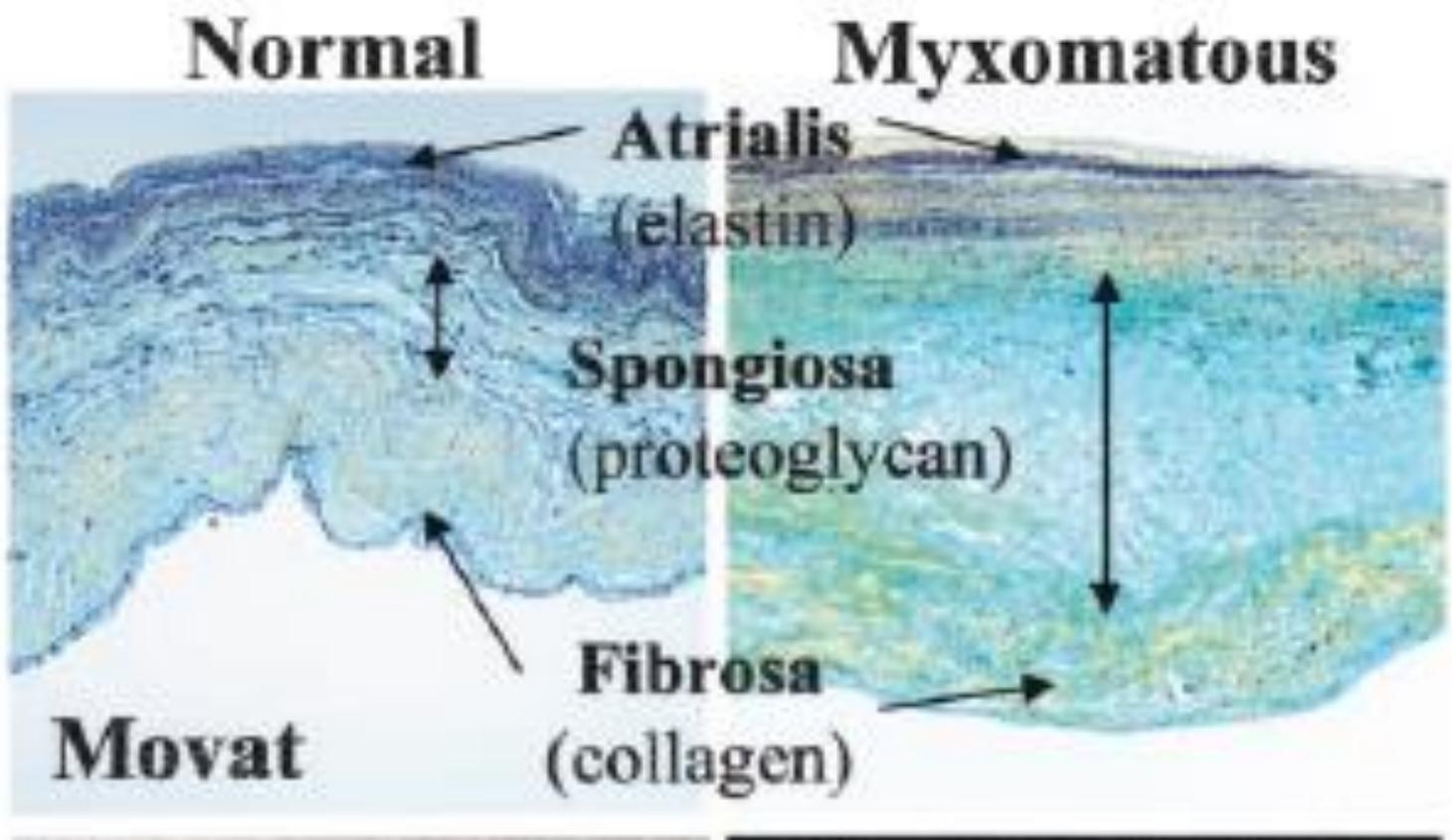
Ballonisation
(Barlow)



Barlow
compliqué de prolapsus



(1) bilan de la dégénérescence myxoïde



Rabkin et al., Circulation 104:2525-32, 2001

Selective transcriptomic profile

	Normal n=4	Myxomatous n=4	t-test
$\alpha 1$ I	100 \pm 29	88 \pm 20	NS
$\alpha 1$ III	100 \pm 43	107 \pm 23	NS
elastin	100 \pm 60	99 \pm 28	NS
fibrillin 1	100 \pm 58	118 \pm 30	NS
fibrillin 2	100 \pm 81	194 \pm 88	0.08
decorin	100 \pm 70	211 \pm 48	<0.02
MMP2	100 \pm 25	97 \pm 21	NS
MMP14	100 \pm 42	115 \pm 33	NS

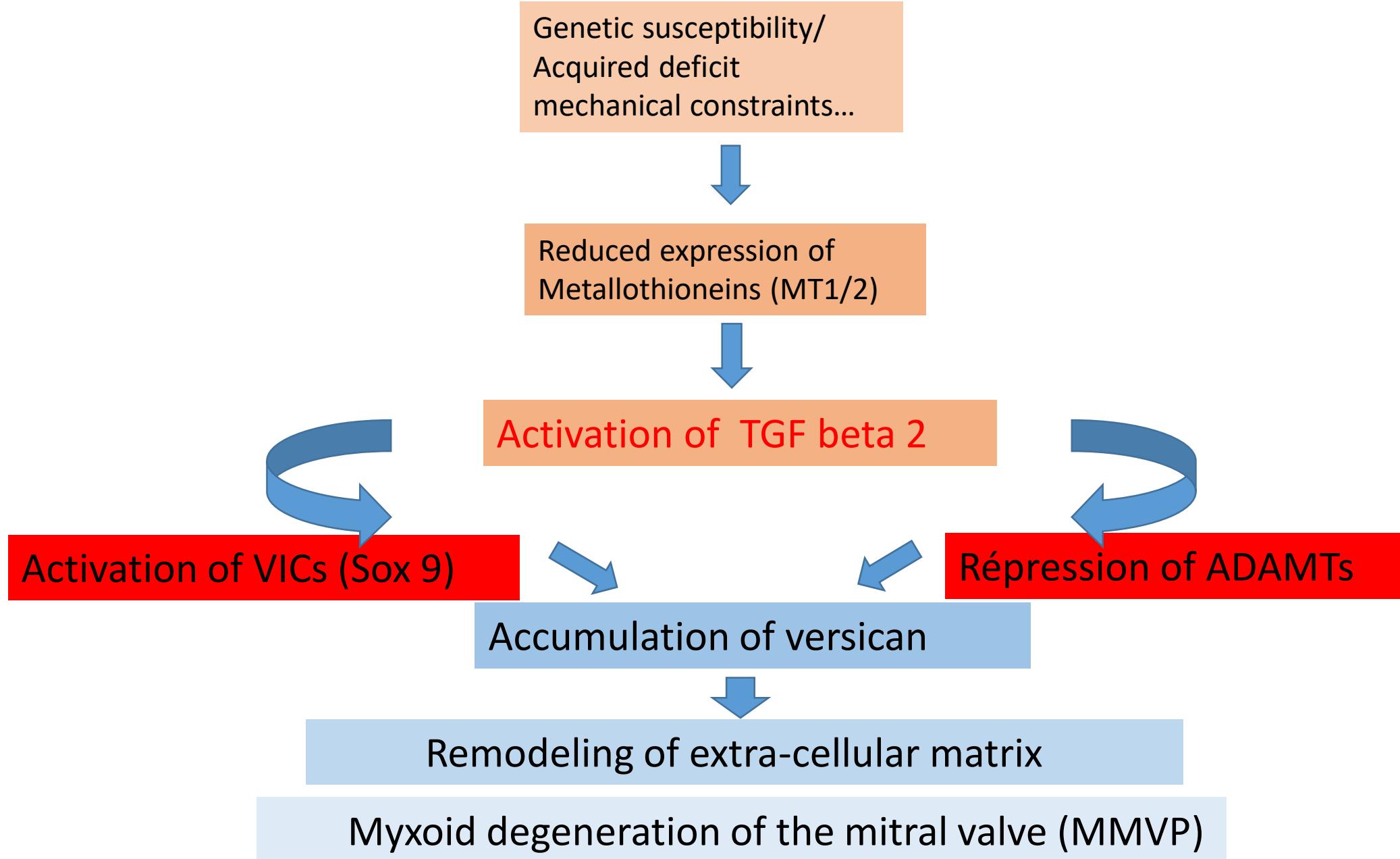
Gènes dont l'expression est modifiée dans la pathologie valvulaire	In vivo	In vitro
Coll $\alpha 1$ I	↗	NS
Coll $\alpha 1$ III	NS	↖
Lumican	↗	NS
Hyaluronan synthase 2	↖	NS
MMP14	↖	NS

Tableau 4.3: Liste des gènes pour lesquels l'expression est modifiée, de manière significative, dans les tissus ou cellules pathologiques, comparativement aux contrôles sains. ↗ : augmentation de l'expression et ↖ : diminution de l'expression dans les valves myxomateuses. NS = non significatif.

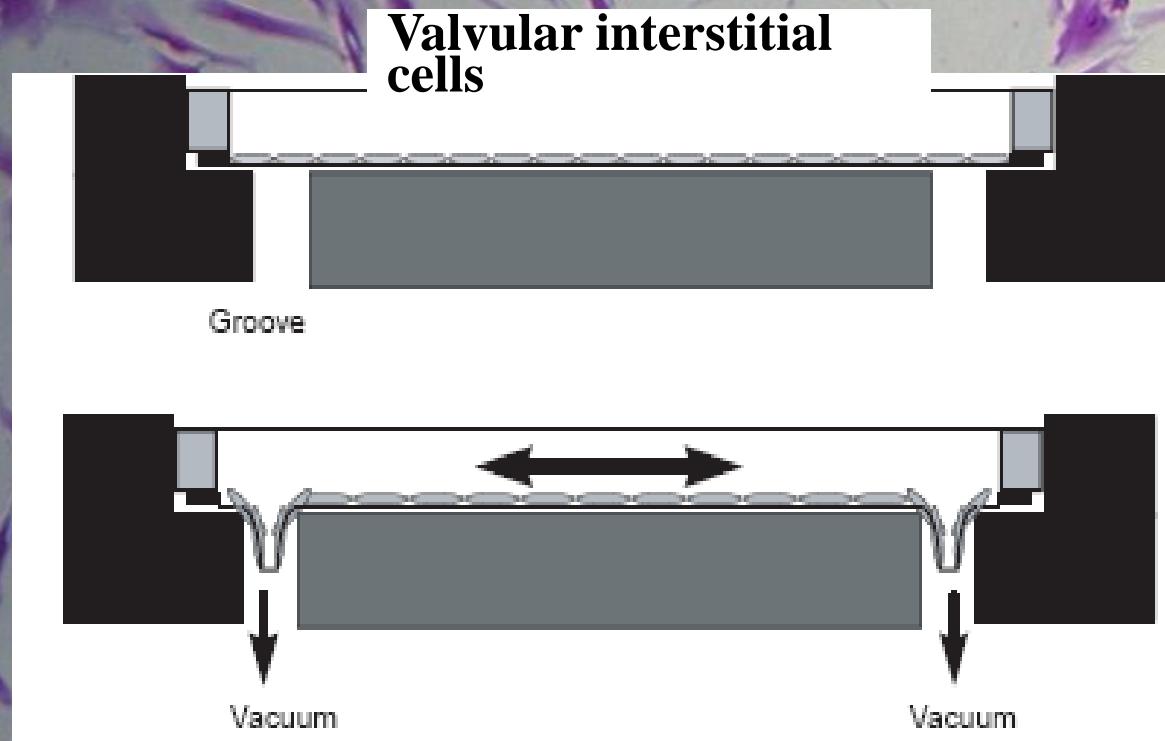
(2)

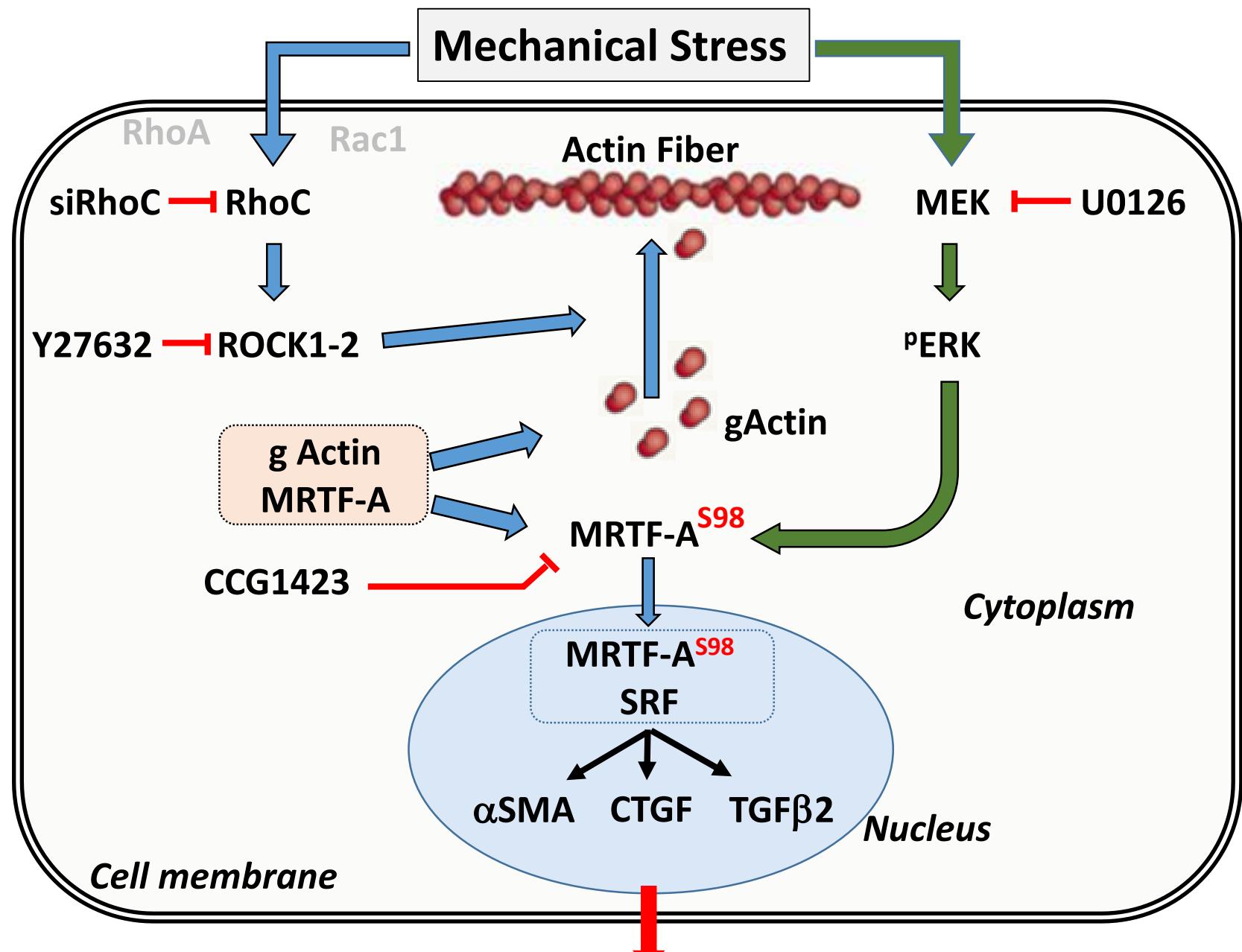
Microarray VMN versus MVVP

Gene	Fold change (MMV vs. control)			
		[1] ^a	[*] ^a	[2] ^a
CD34	CD34 molecule		1.7	
<i>Extracellular matrix</i>				
IGF- β 2	Transforming growth factor beta 2	1.7		
LTBP4	Latent transforming growth factor beta binding protein 4	2.6	8.0	
BMP4	Bone morphogenetic protein 4	2.3	8.0	
SOX 9	SRY (sex determining region Y)-box 9	1.4	6.0	
COMP	Cartilage oligomeric matrix protein		6.7	
CRTAC1	Cartilage acidic protein 1		21	
SPP1	Osteopontin	−3.3		
BGN	Biglycan		4.1	
DCN	Decorin		2.1	
VSCN	Versican		3.0	
XYLT-I	Xylosyltransferase I	1.6		
ADAMTS-1	ADAM metallopeptidase with thrombospondin type 1 motif, 1	−2.5		
ADAMTS-5	ADAM metallopeptidase with thrombospondin type 1 motif, 5	−3.3		
ADAMTS-9	ADAM metallopeptidase with thrombospondin type 1 motif, 9	−2.0		
<i>Antioxidant system</i>				
MT1E	Metallothionein 1E	−3.2		
MT1F	Metallothionein 1F	−5.7		
MT1G	Metallothionein 1G	−4.6		
MT1M	Metallothionein 1M	−6.5		
MT1P2	Metallothionein 1 pseudogene 2	−3.3		
MT1X	Metallothionein 1X	−4.6		
MT2A	Metallothionein 2A	−3.2		
NQO1	NAD(P)H dehydrogenase, quinone 1		−2.0	
SOD2	Superoxide dismutase 2	−4.9		
GLRX	Glutaredoxin (thioltransferase)	−2.3		
TXN	Thioredoxin		−1.7	

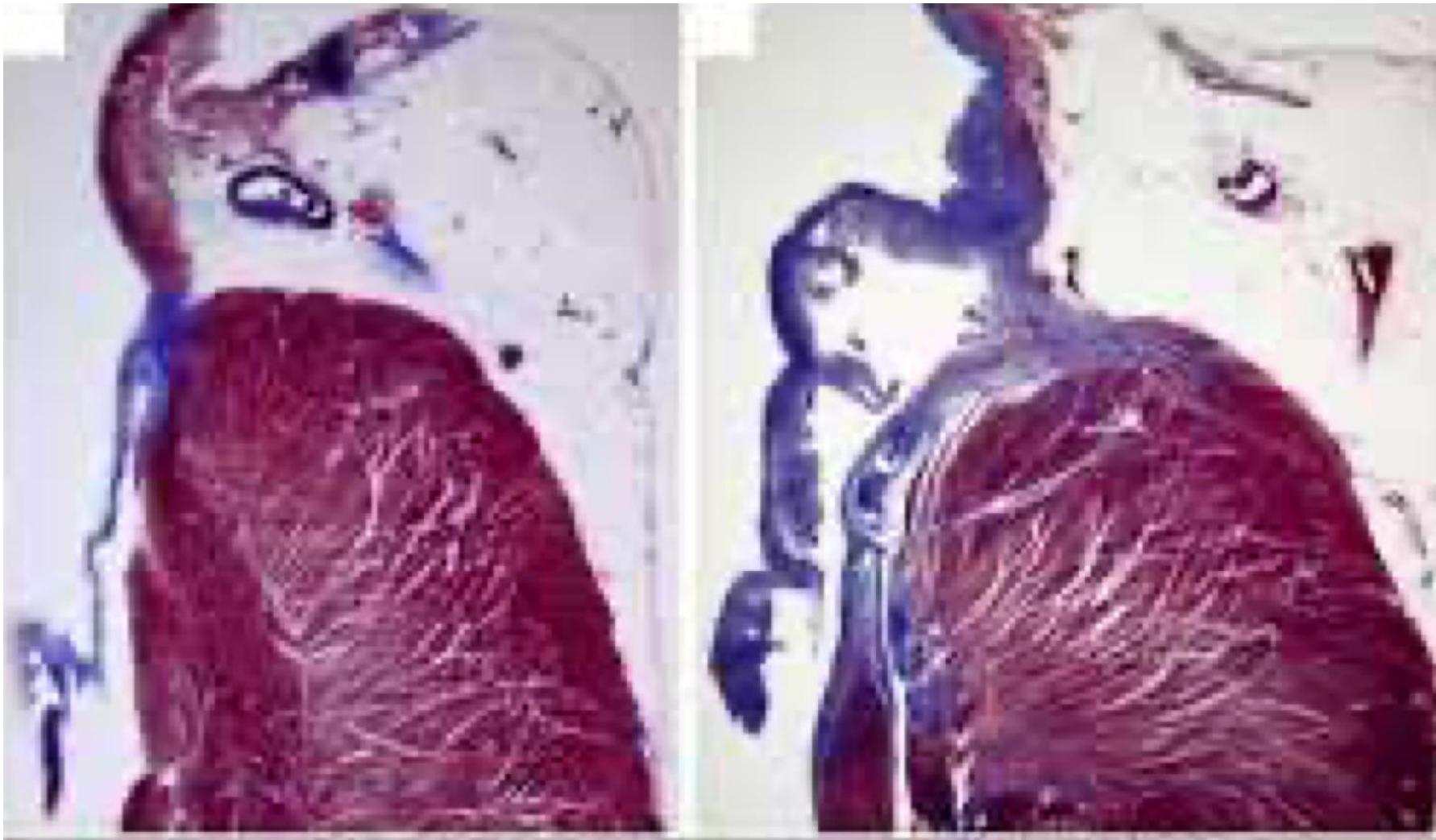


VICs submitted to cyclic mechanical constraints



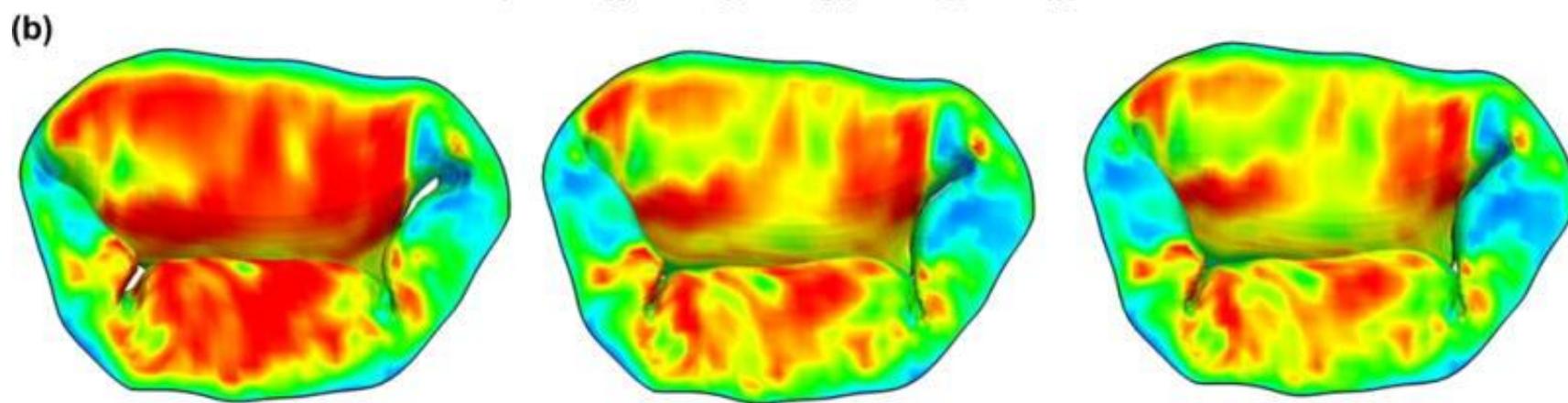
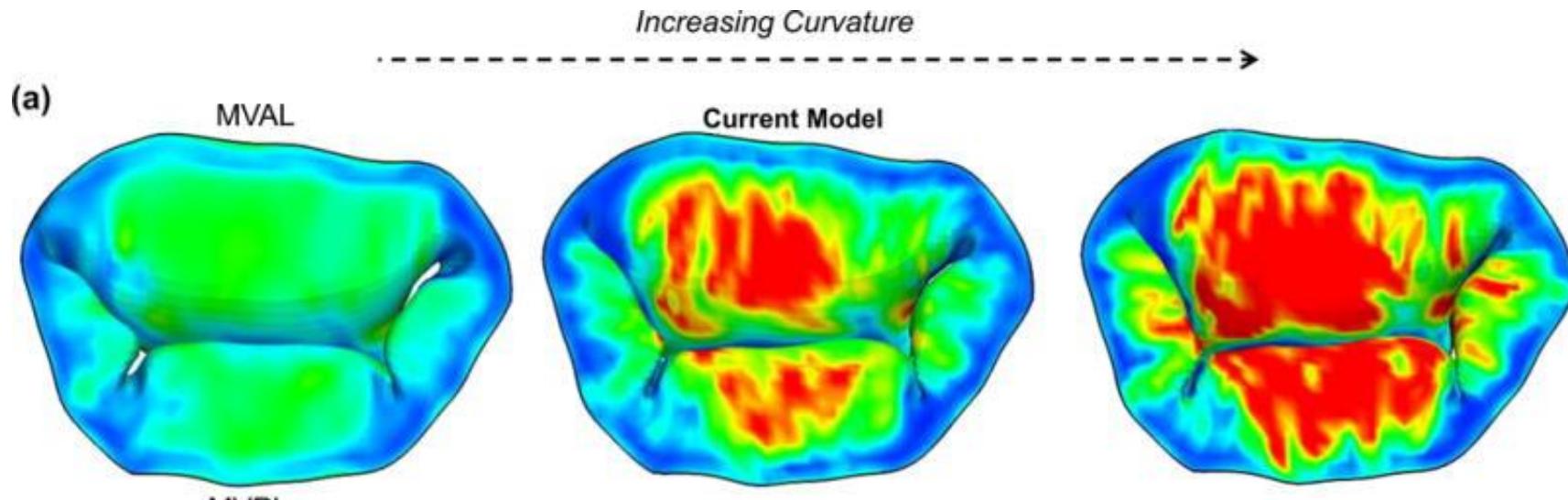


Normal AV junction versus... MAD





Histological section from the region of the mitral annulus showing a wide separation between the insertion of mitral valve and the left ventricular top border (arrowheads). Reproduced with permission from Hutchins GM, Moore GW, Skoog DK. "The association of floppy mitral valve with disjunction of the mitral annulus fibrosus". N Engl J Med 1986; 314: 535-540.



1 - Pathological movement of mitral valve annulus in Barlow's disease

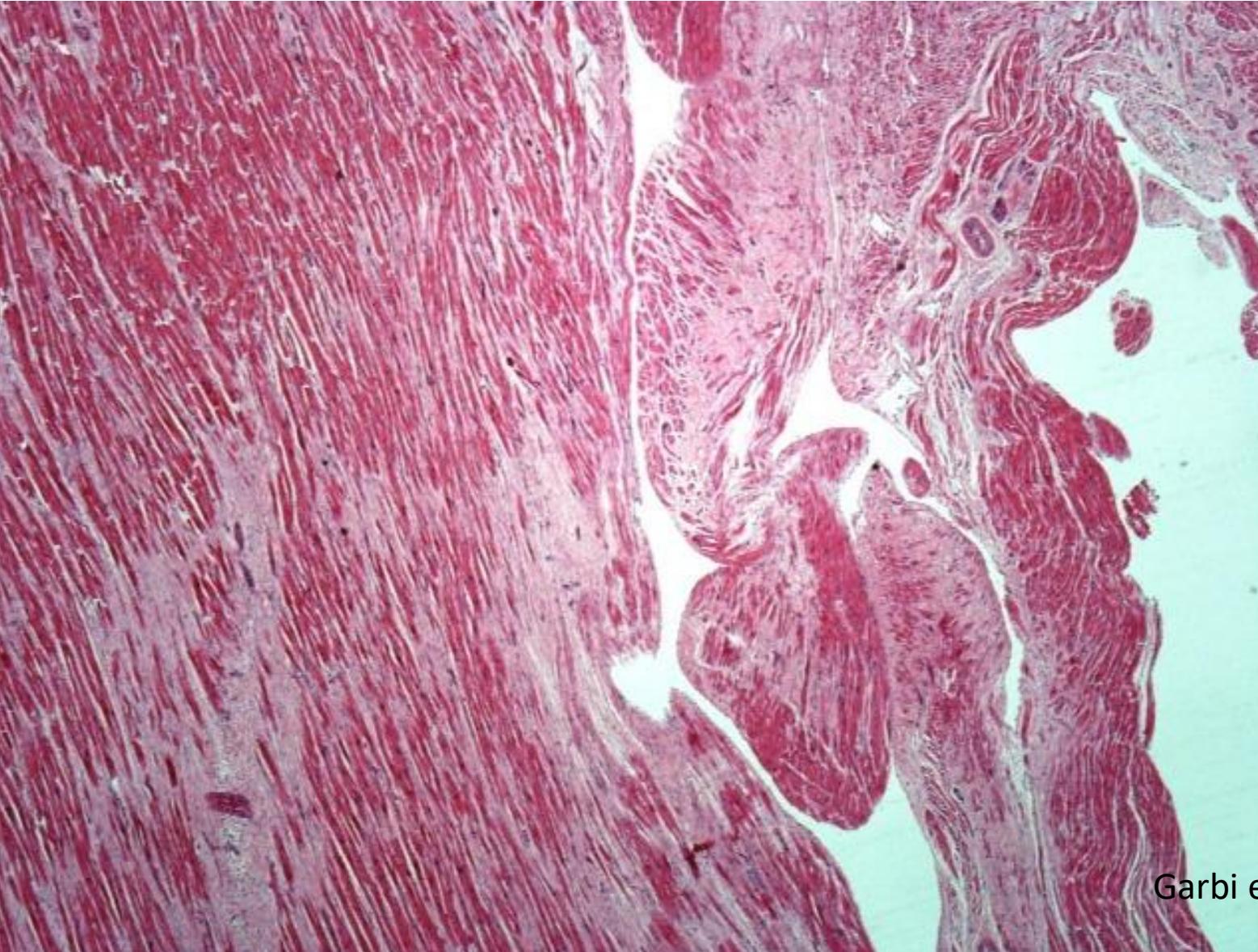
To sum up:

- Myxomatous degeneration / remodeling is the common denominator of most valve lesions and dysfunctions in degenerative mitral valve disease
- Myxoid degeneration is better understood . Controlling the remodeling of the valve becomes (theoretically) realistic
- Stress is likely the culprit of most valve lesions (excess tissue, thickening, billowing, MAD) seen in our practice which will eventually lead to valve dysfunction

Anomaly & features and physio-path of Barlow disease

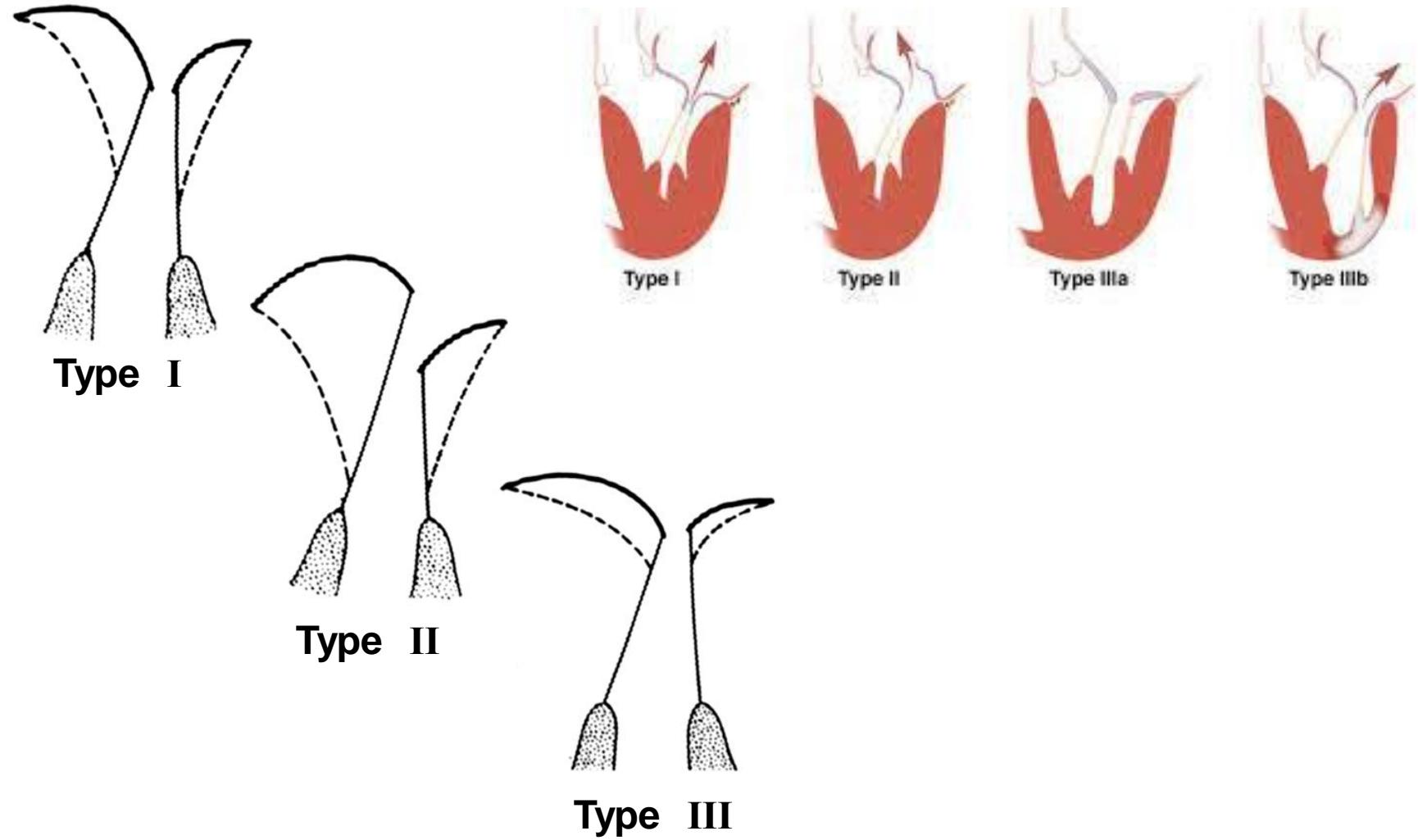
- 1963 (Am H J) Barlow: “ late systolic murmur and non ejectional click”
- 1964 Segall &Likoff “systolic bulging of anterior leaflet associated to onset of MR”
- 1966 (Am H J) Barlow &Bosman report 4 patients with mid systolic click and late mitral murmur with the posterior leaflet undergoing massive protrusion into the LA which they described as “aneurysmal or billowing”
- 1968 Ehlers et al : left ventricular wall motion abnormalities “systolic contraction ring” but wrong interpretation
- 1973 Liedtke /Scampardonis : “papillary muscle moves in systole towards the mitral annulus instead of the apex”
- 1975 (circulation) Nutter et al: establish the physiopathology of idiopathic mitral valve prolapse

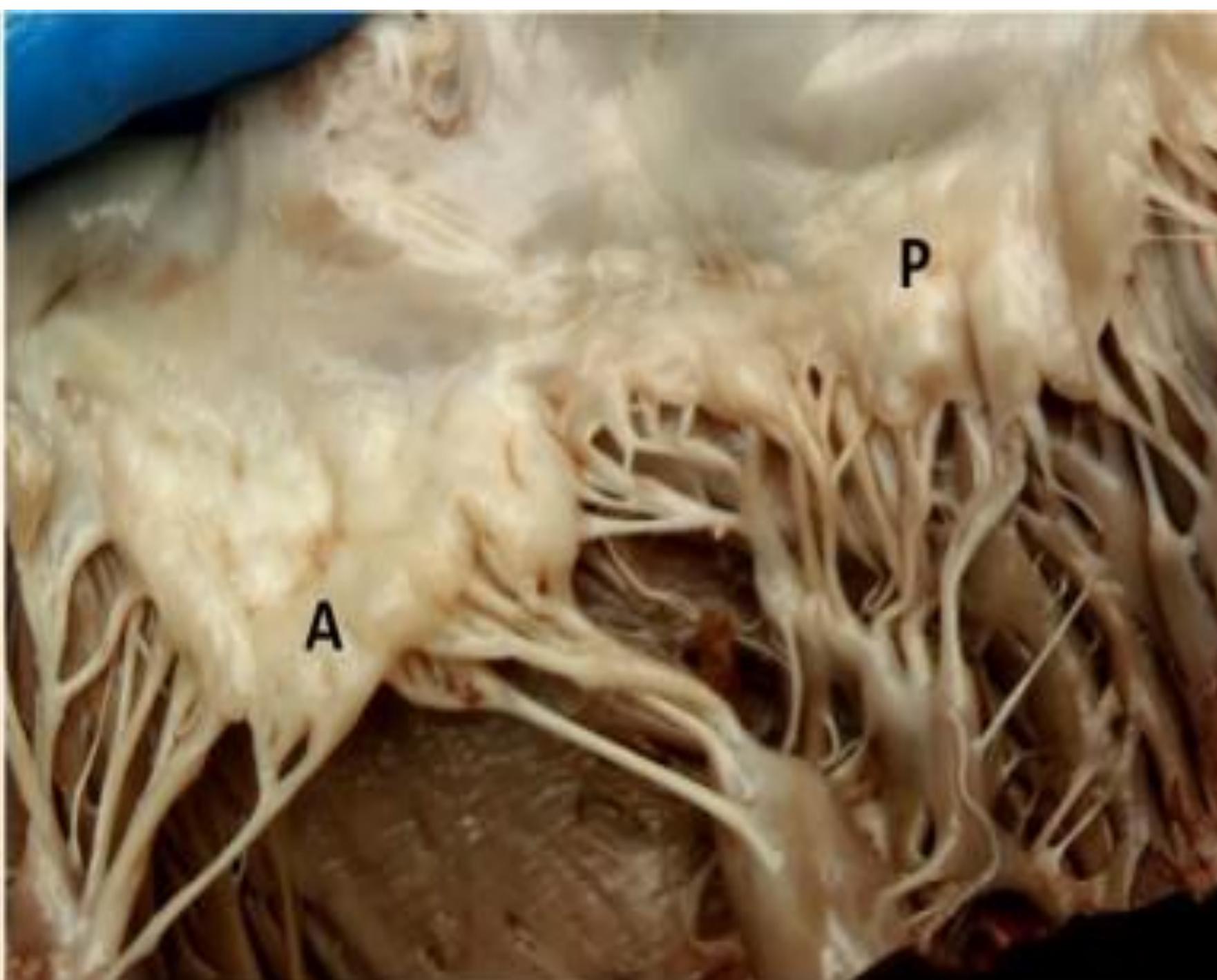
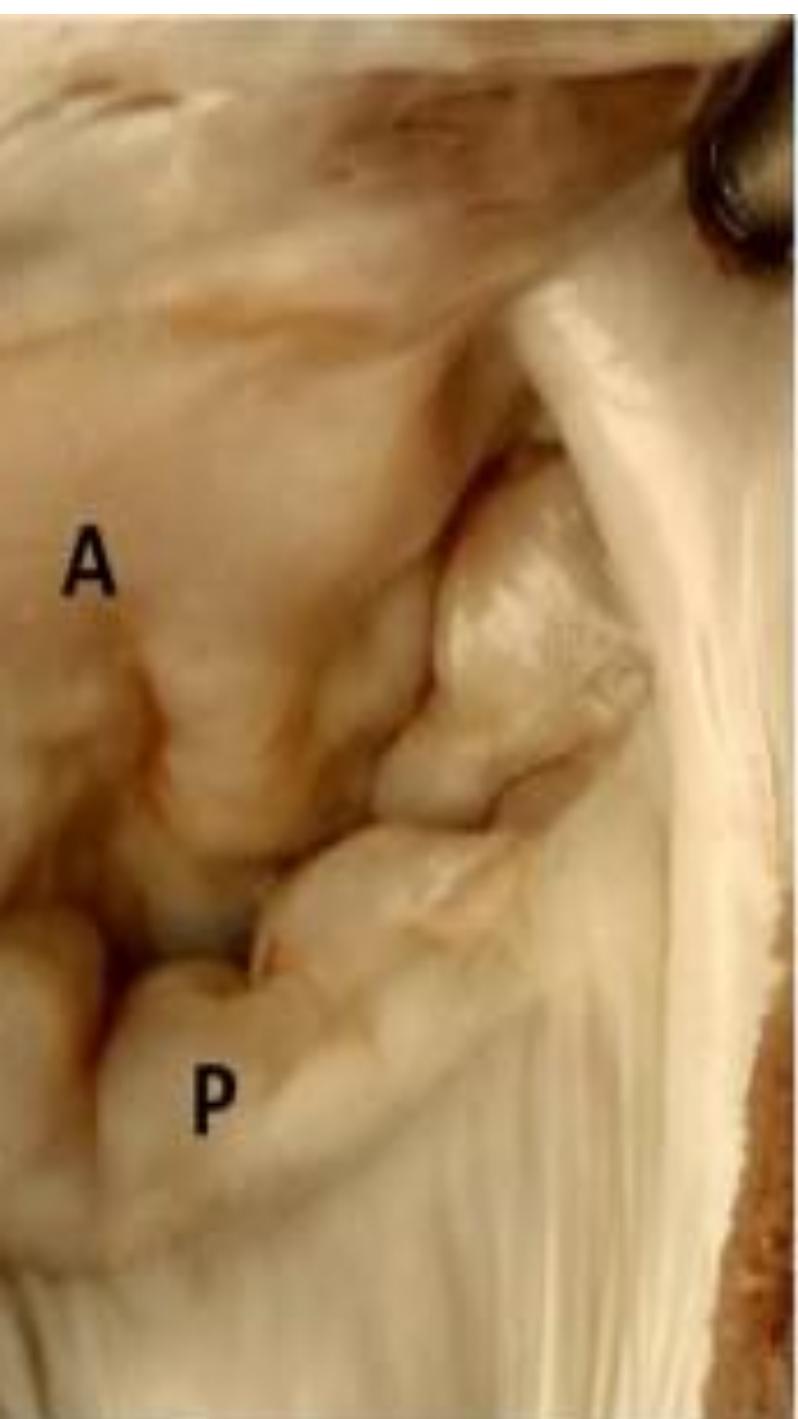
Myocardial Fibrosis in Malignant MVP/Barlow disease

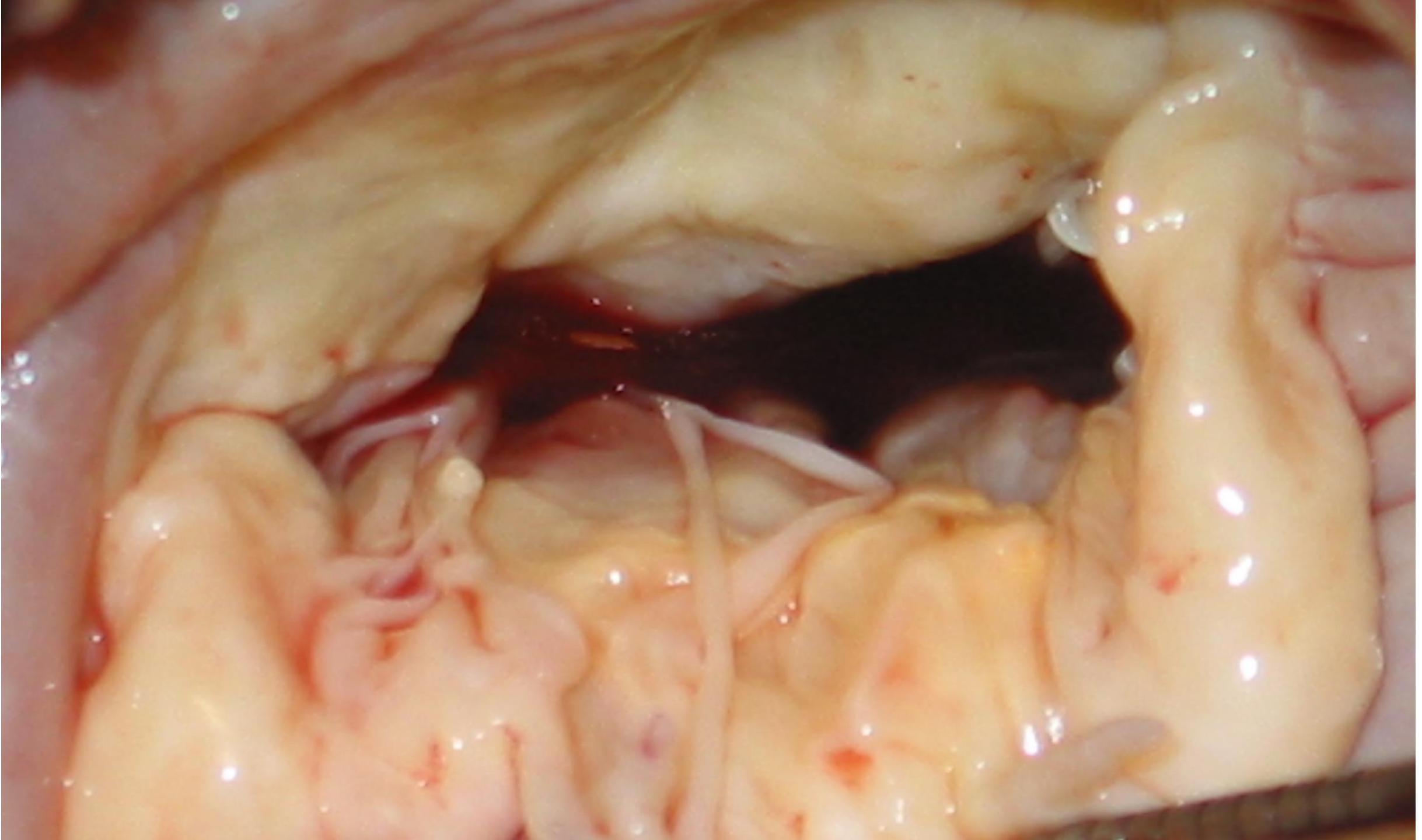


Garbi et al open heart 2018

Classification Fonctionnelle de Carpentier







- N Engl J Med. 1986 Feb 27;314(9):535-40.
- **The association of floppy mitral valve with disjunction of the mitral annulus fibrosus.**
Hutchins GM, Moore GW, Skoog DK.
- Floppy mitral valve is usually attributed to connective-tissue degeneration. However, we have observed several instances in which both a floppy mitral valve and an abnormal mitral annulus fibrosus were present at autopsy. To study this association, we examined 900 hearts (after postmortem arteriography and fixation in distention) from autopsies of adults at The Johns Hopkins Hospital. Twenty-five (3 percent) of the hearts had a morphologically typical floppy mitral valve; in 23 of them (92 percent), the mitral annulus fibrosus showed disjunction--i.e., a separation between the atrial wall-mitral valve junction and the left ventricular attachment. In 42 other hearts (5 percent), which were from significantly younger patients (mean age [$+$ / $-$ SE], $60 +/ - 2$ years vs. $68 +/ - 3$; P less than 0.05), there was mitral annulus disjunction but no floppy mitral valve. Two hearts had a floppy mitral valve but no disjunction of the annulus; both of them had old infarcts of the papillary muscle. Our results show that floppy mitral valve is significantly associated with disjunction of the mitral annulus fibrosus (P less than 0.001). We suggest that floppy mitral valve develops from hypermobility of the valve apparatus, and that it is usually secondary to disjunction of the mitral annulus fibrosus, an anatomic variation in the morphology of the annulus.
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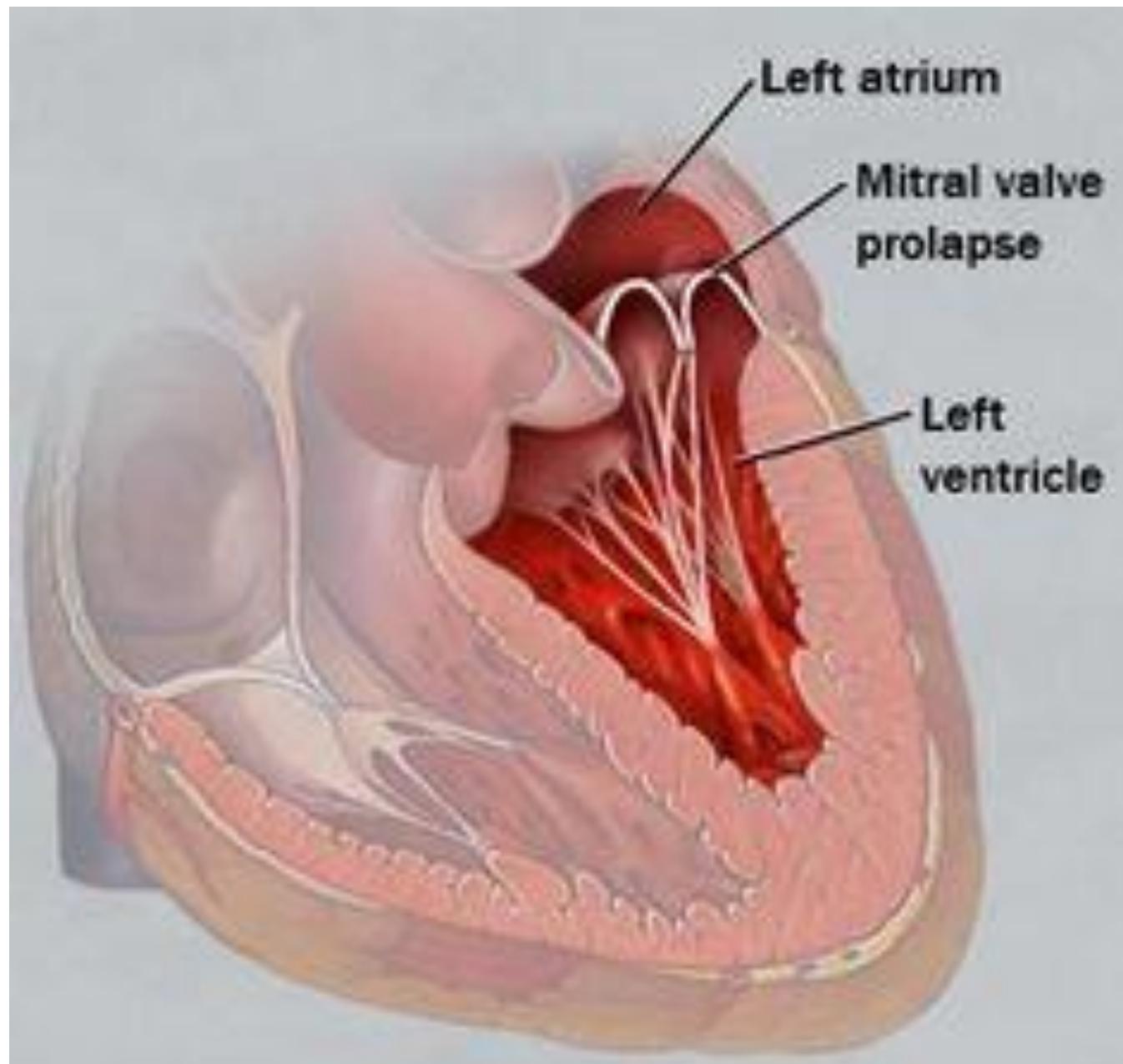
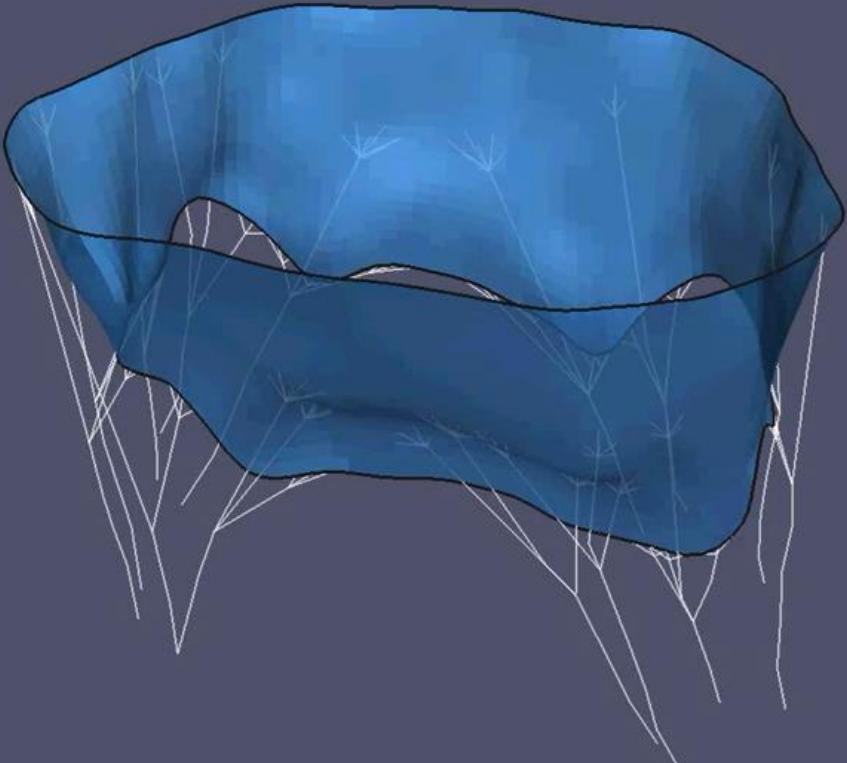
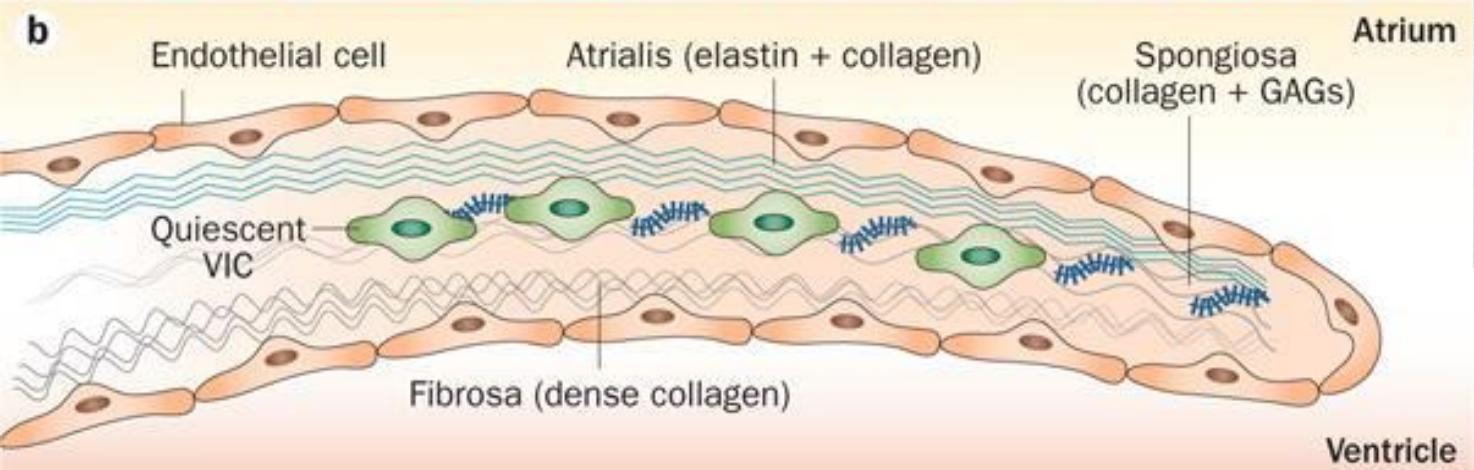
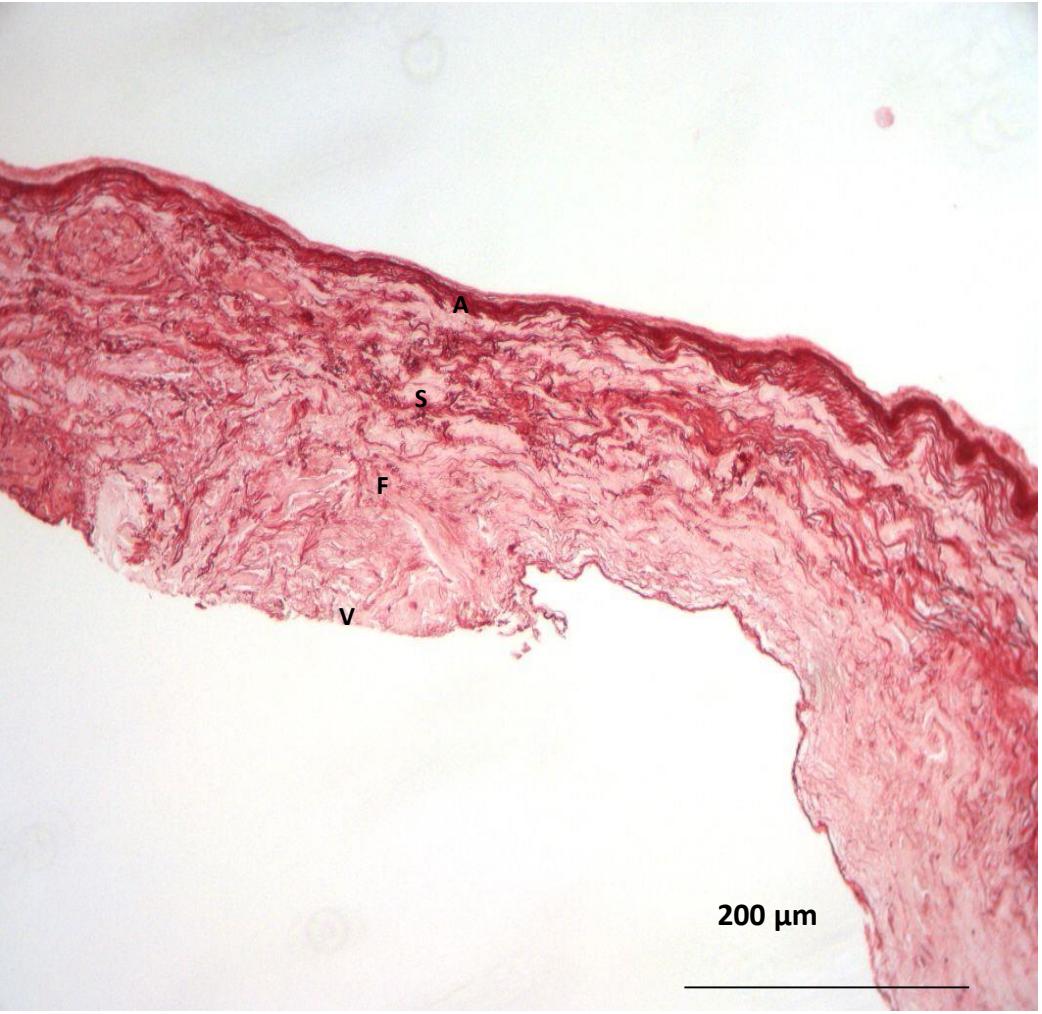
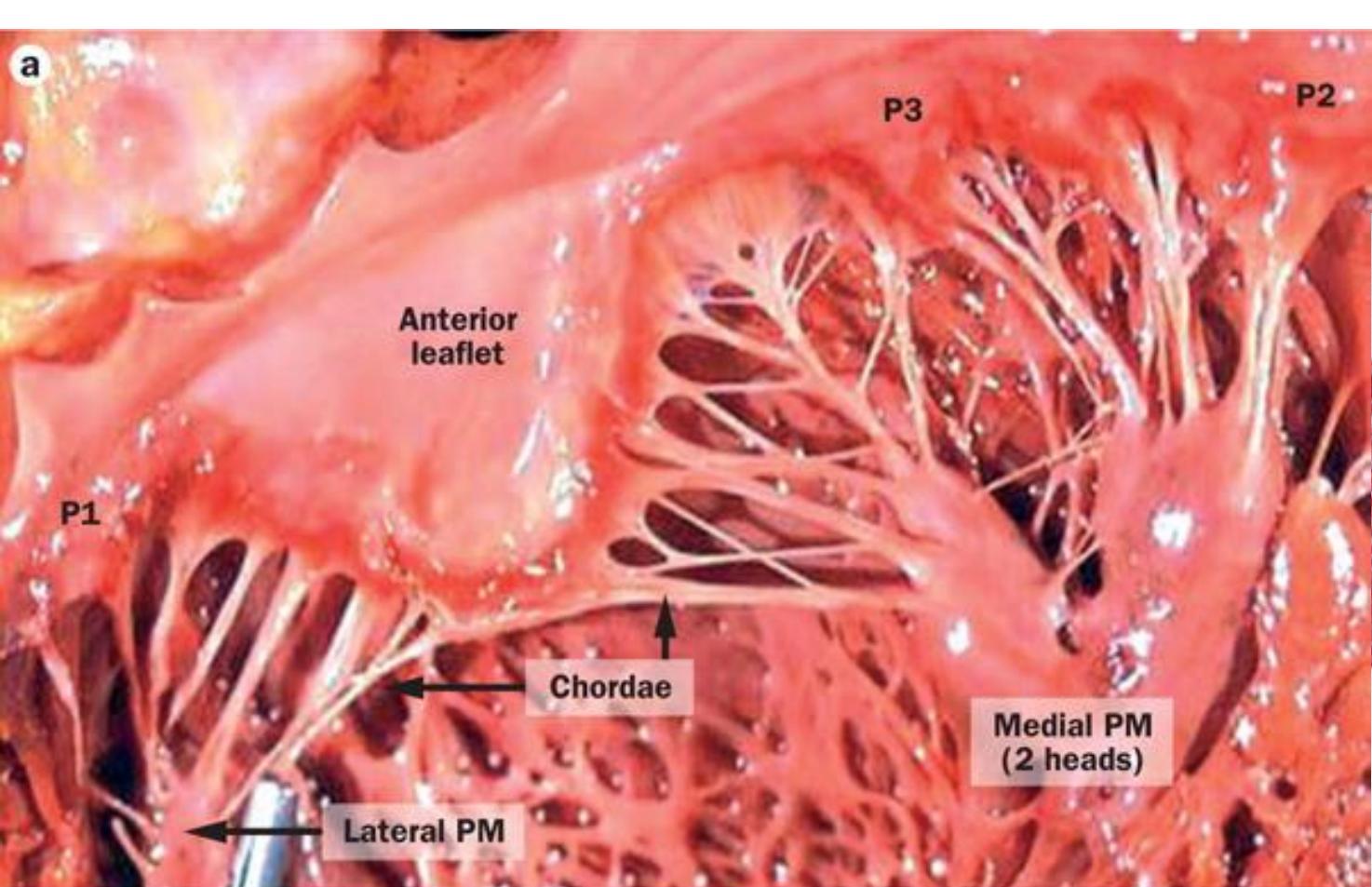


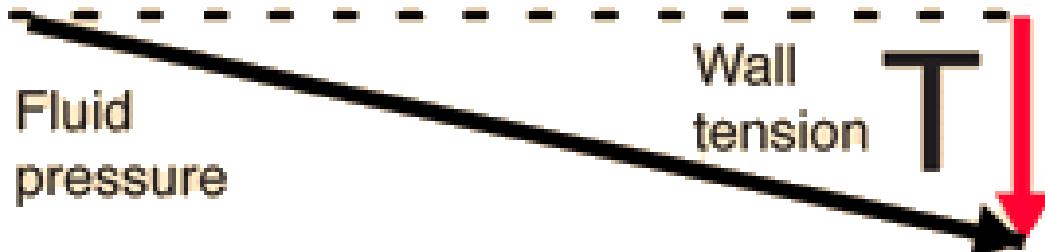
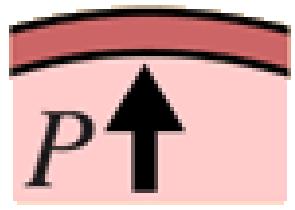
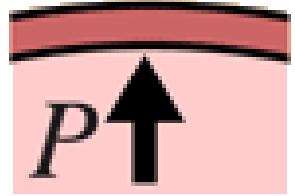


Image-Based Reconstruction of Mitral Valve Finite Element Model

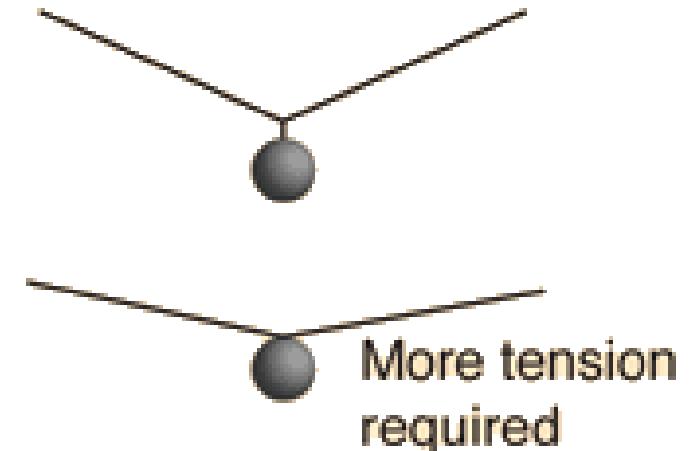


Chung-Hao Lee and Michael Sacks, ICES' Center For Cardiovascular
[Simulationyoutube.com/watch?v=vcxeAwL-fw](https://www.youtube.com/watch?v=vcxeAwL-fw)





For the same internal pressure, the downward component of the tension must be the same.



Analogy: to hang a mass on a cable with less sag, you have to put more tension in the cable.

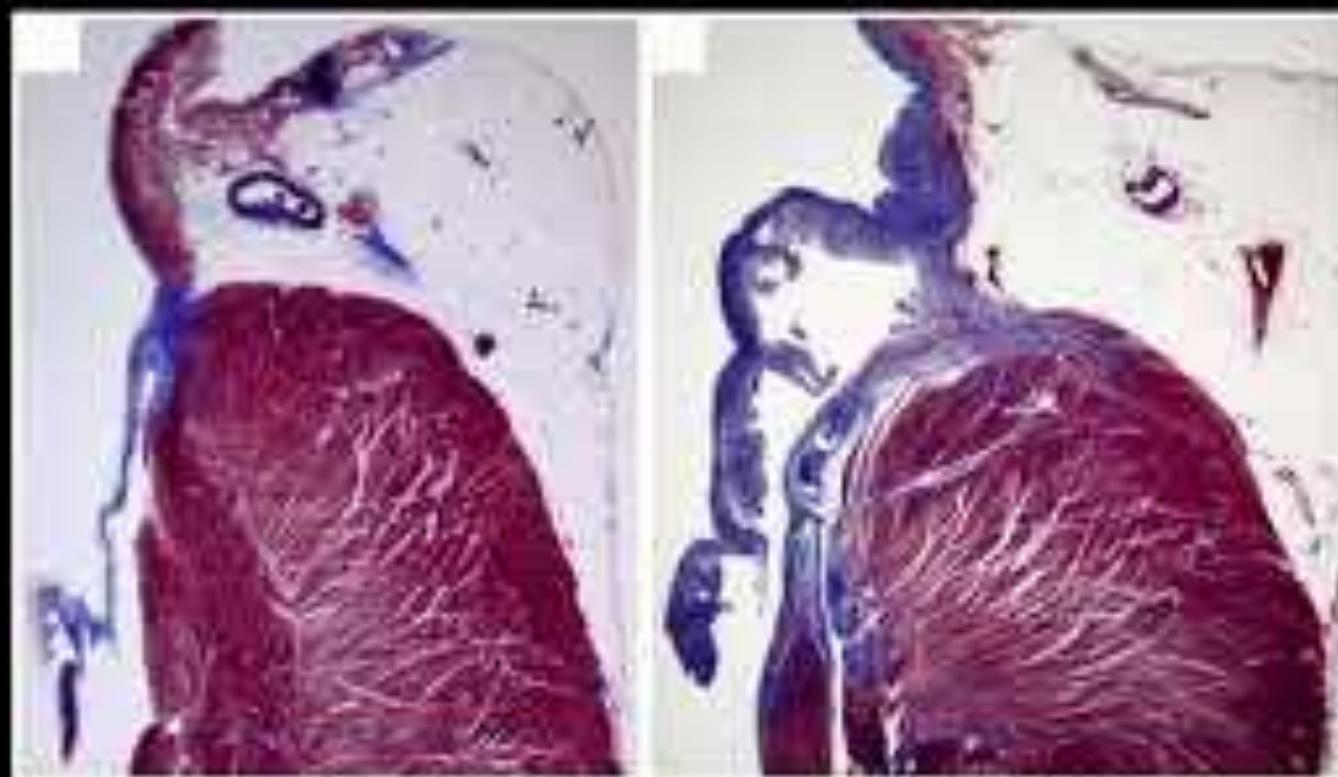


ARRHYTHMIC MITRAL VALVE
PROLAPSE

MARC A. MILLER, MD

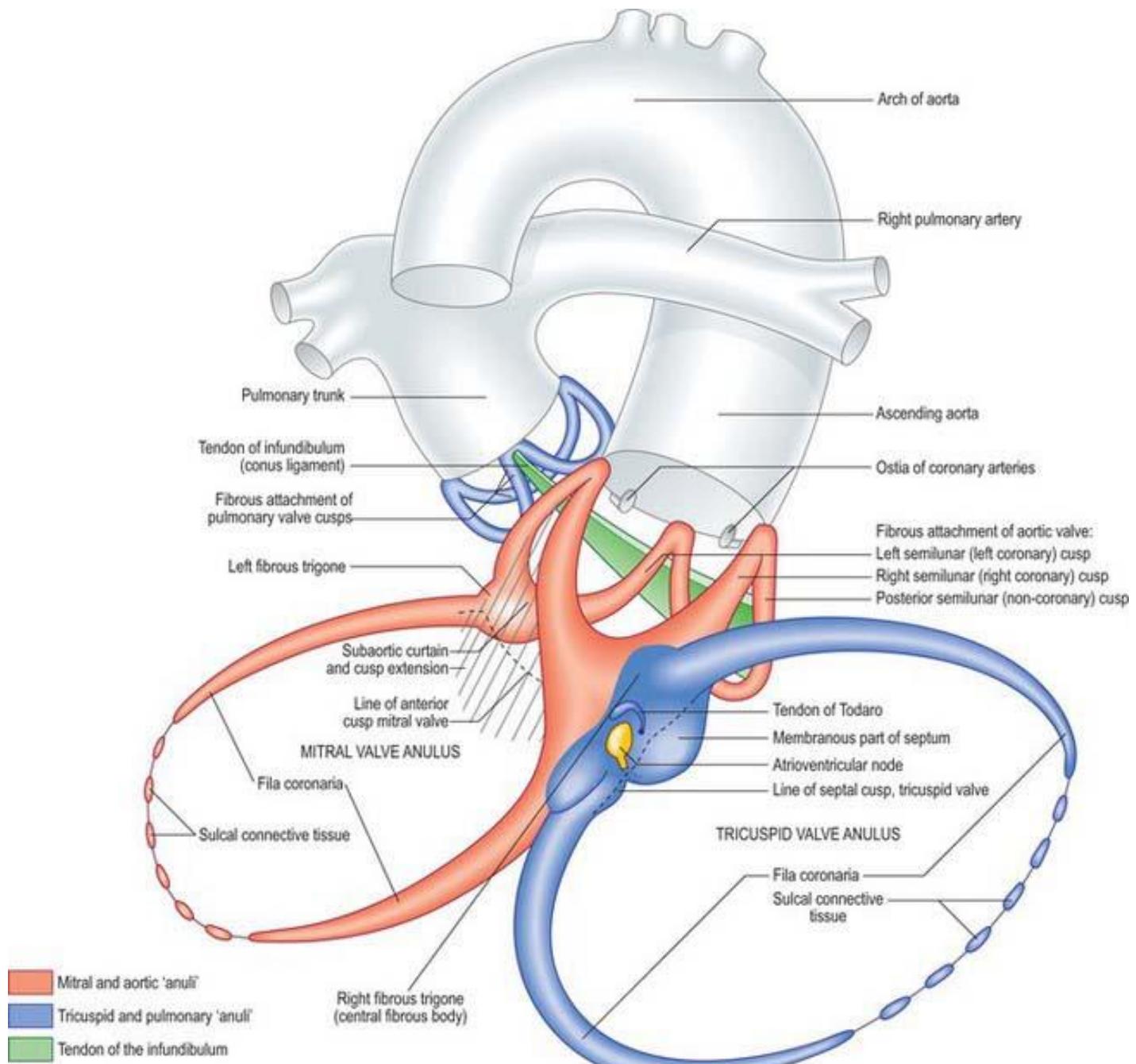
ASSISTANT PROFESSOR OF MEDICINE
CARDIAC ARRHYTHMIA SERVICE

Why do MVP Patients Develop Fibrosis? It is most likely stretch-induced



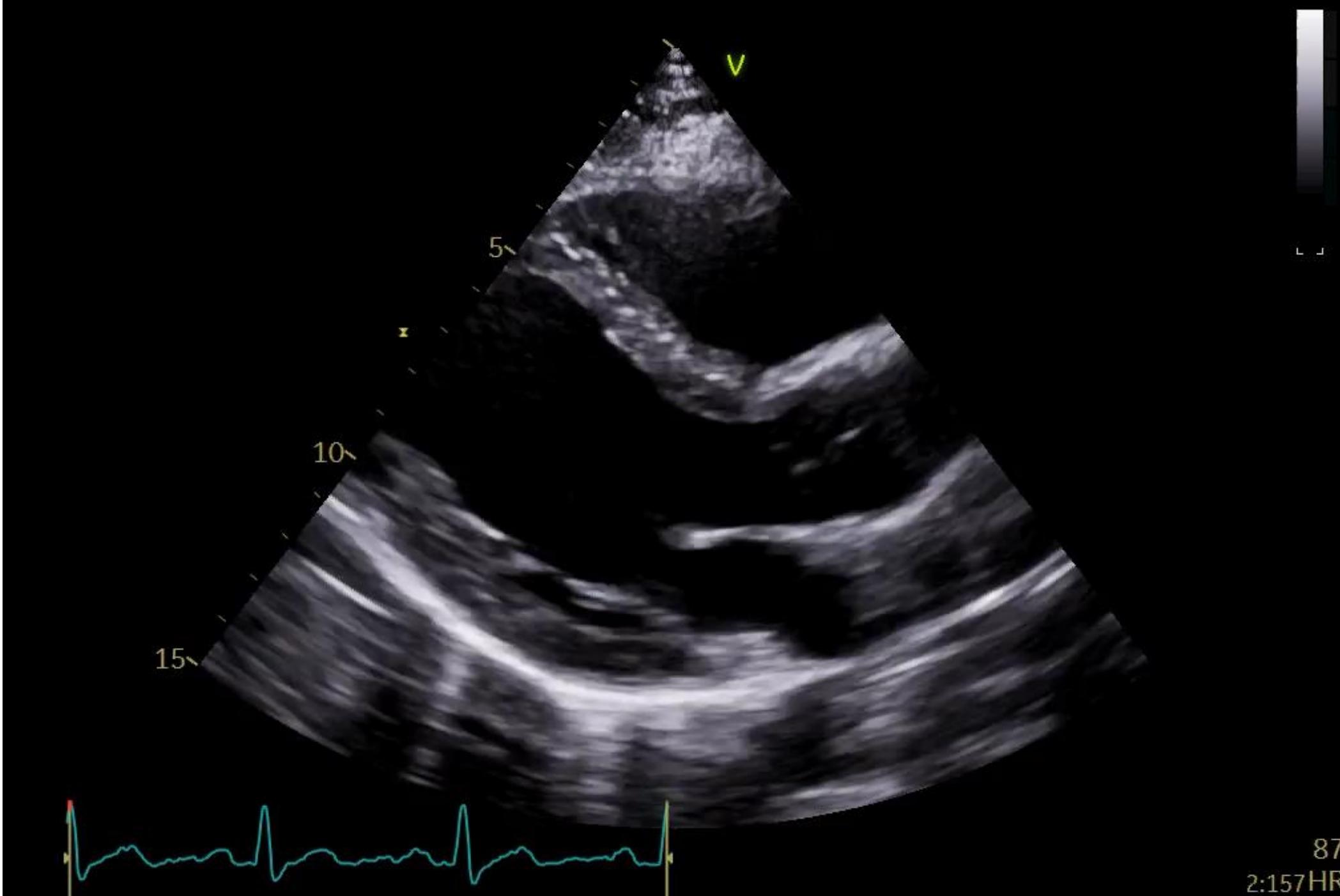
Normal Control

MVP with SCD

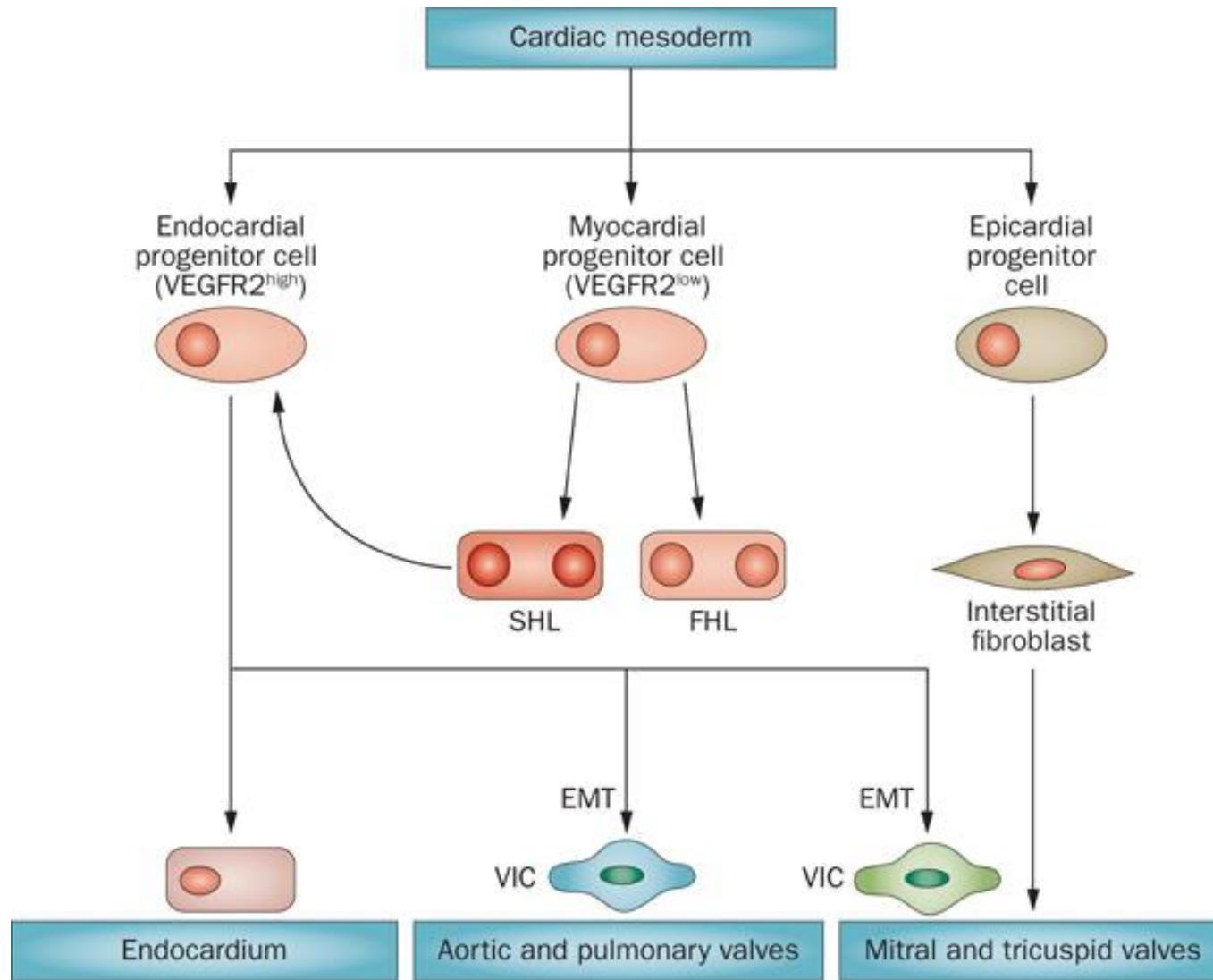


Zimmerman & Bailey, 1962

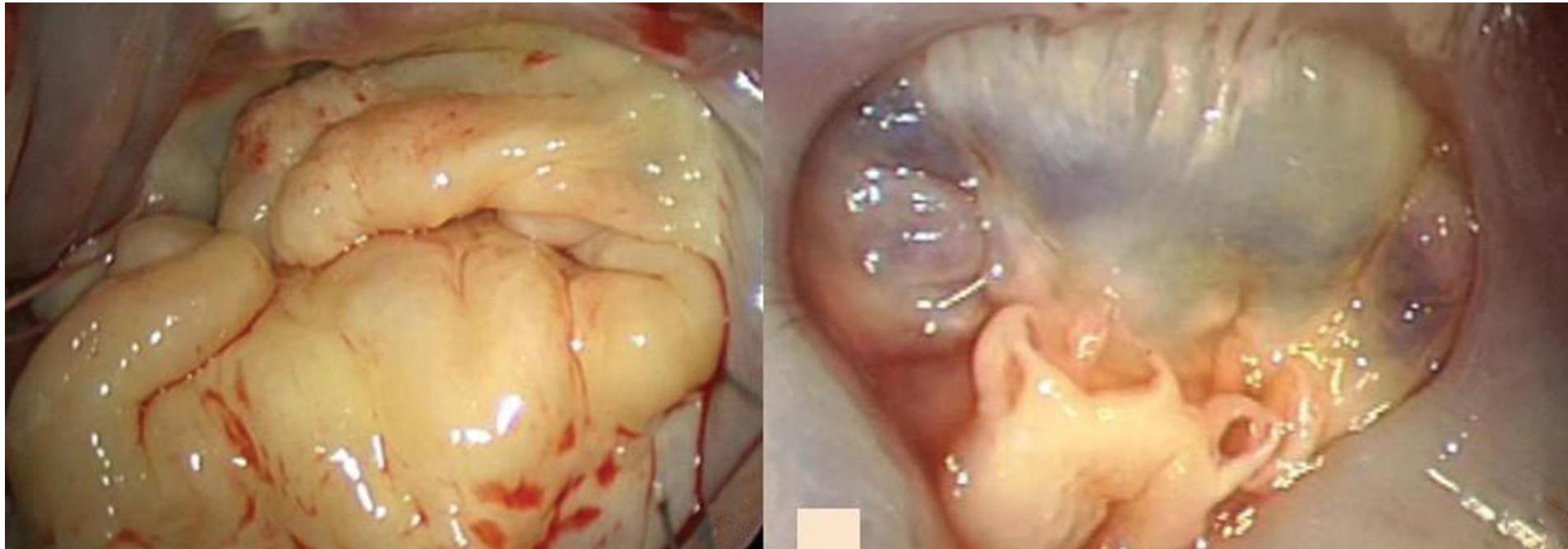
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Formation des VIC's par EMT



La dégénérescence valvulaire myxoïde des feuillets (MMVP)



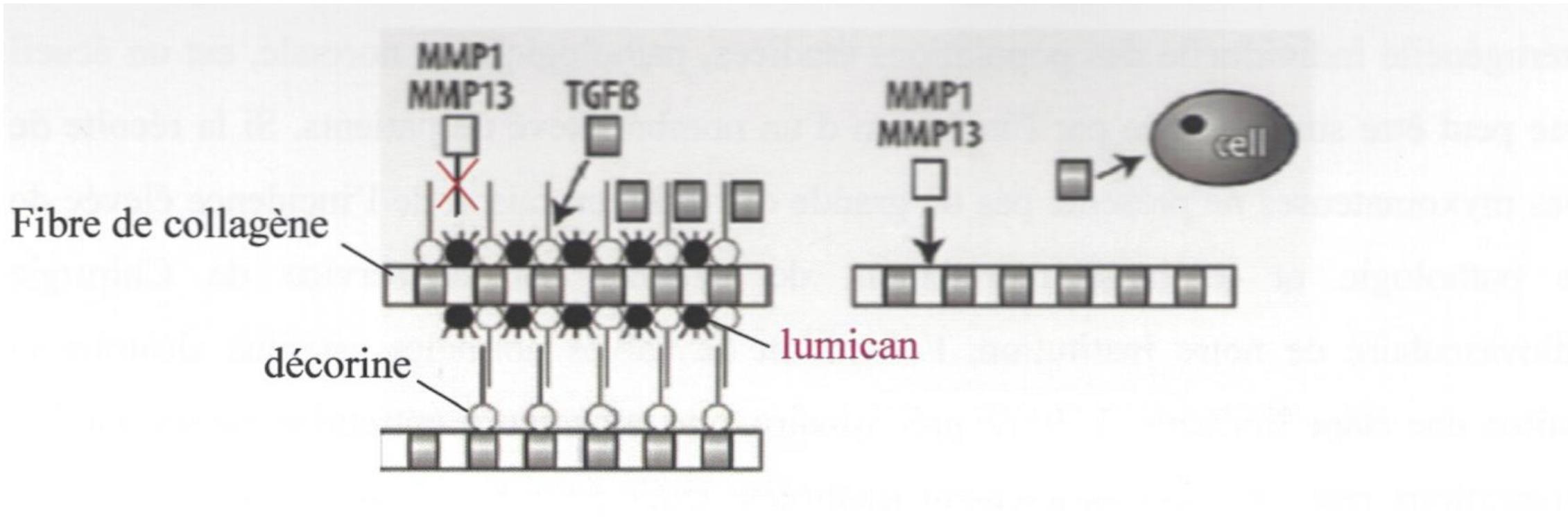
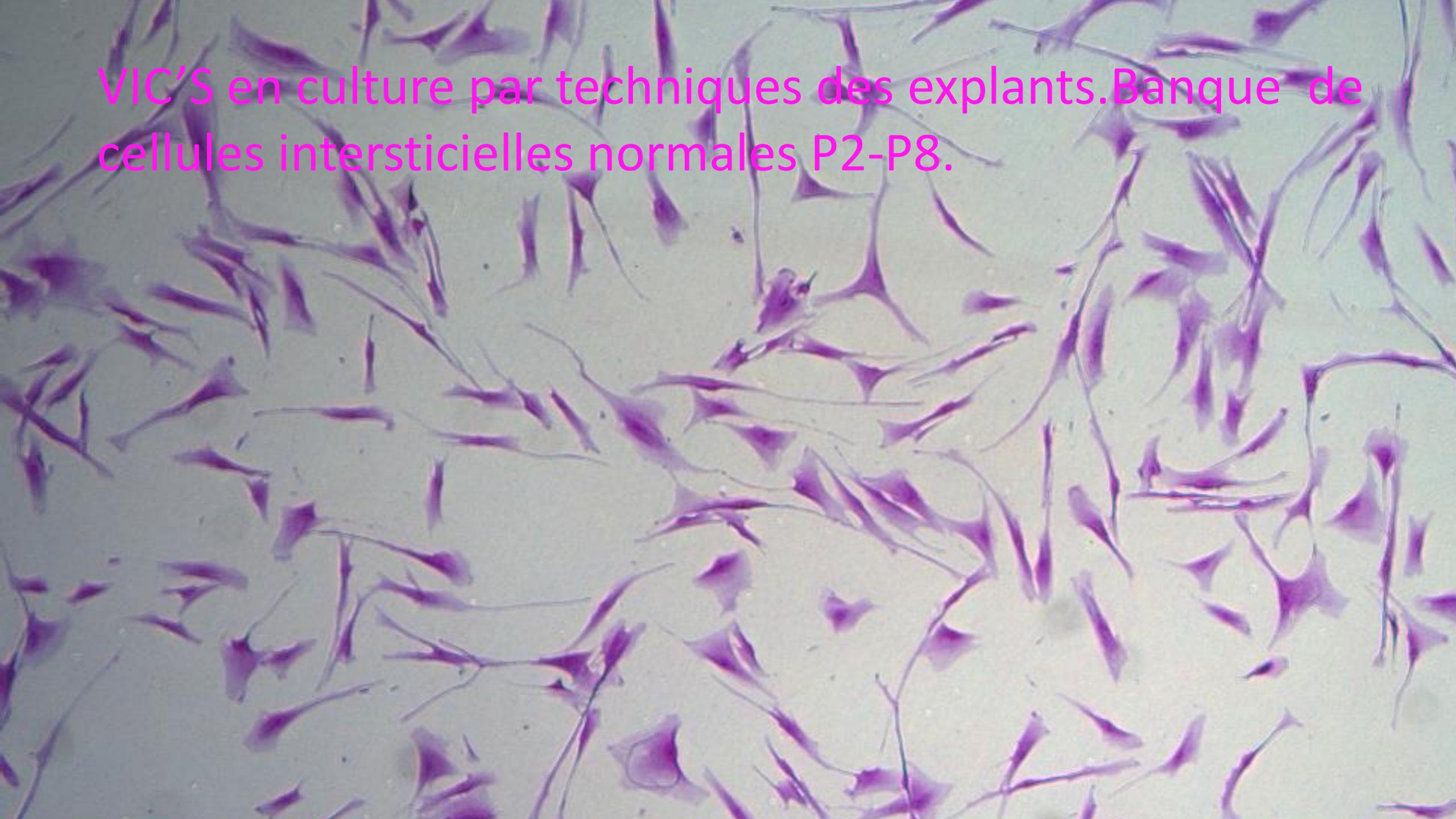
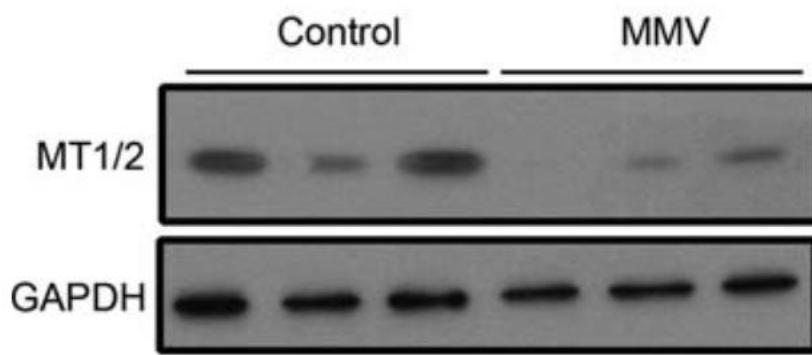


Figure 5.1 : Le lumican, ainsi que la décorine, interagissent avec des régions distinctes du collagène fibrillaire. Ces protéoglycans séquestrent des facteurs de croissance, dont le TGF β 1 et par ailleurs, interfèrent avec l'action des métalloprotéases retardant ainsi la dégradation des fibres.

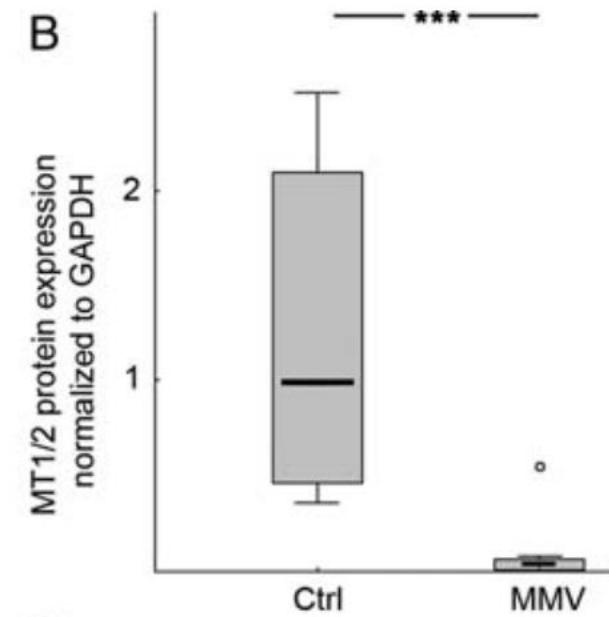
VIC'S en culture par techniques des explants.Banque de cellules interstielles normales P2-P8.



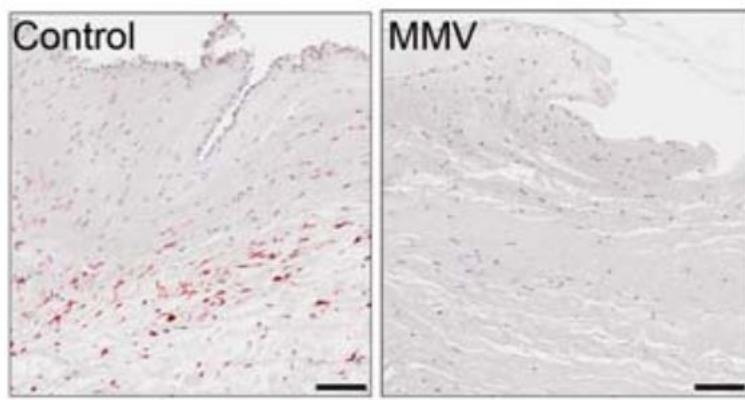
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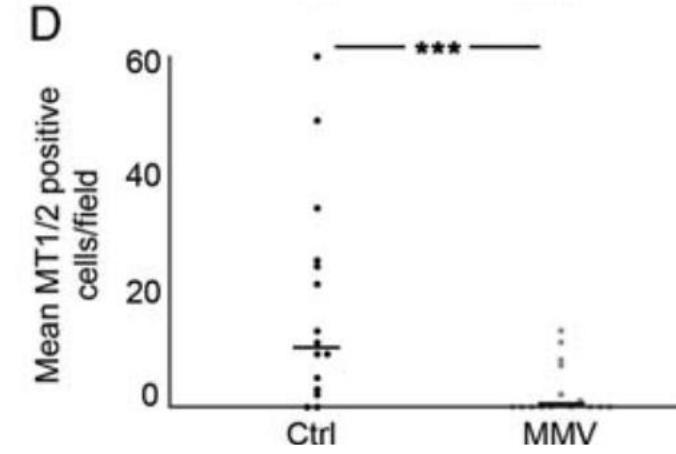
B



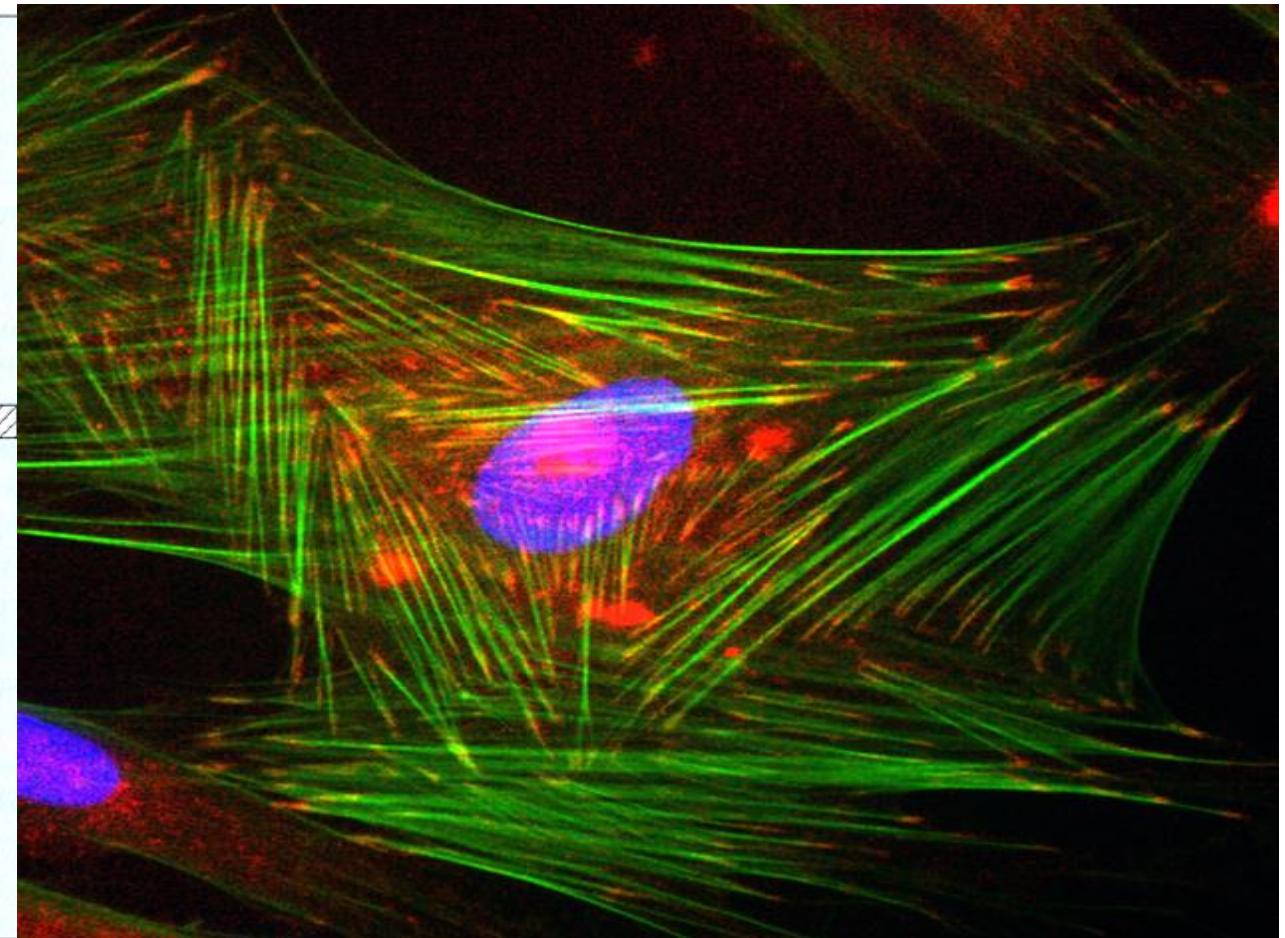
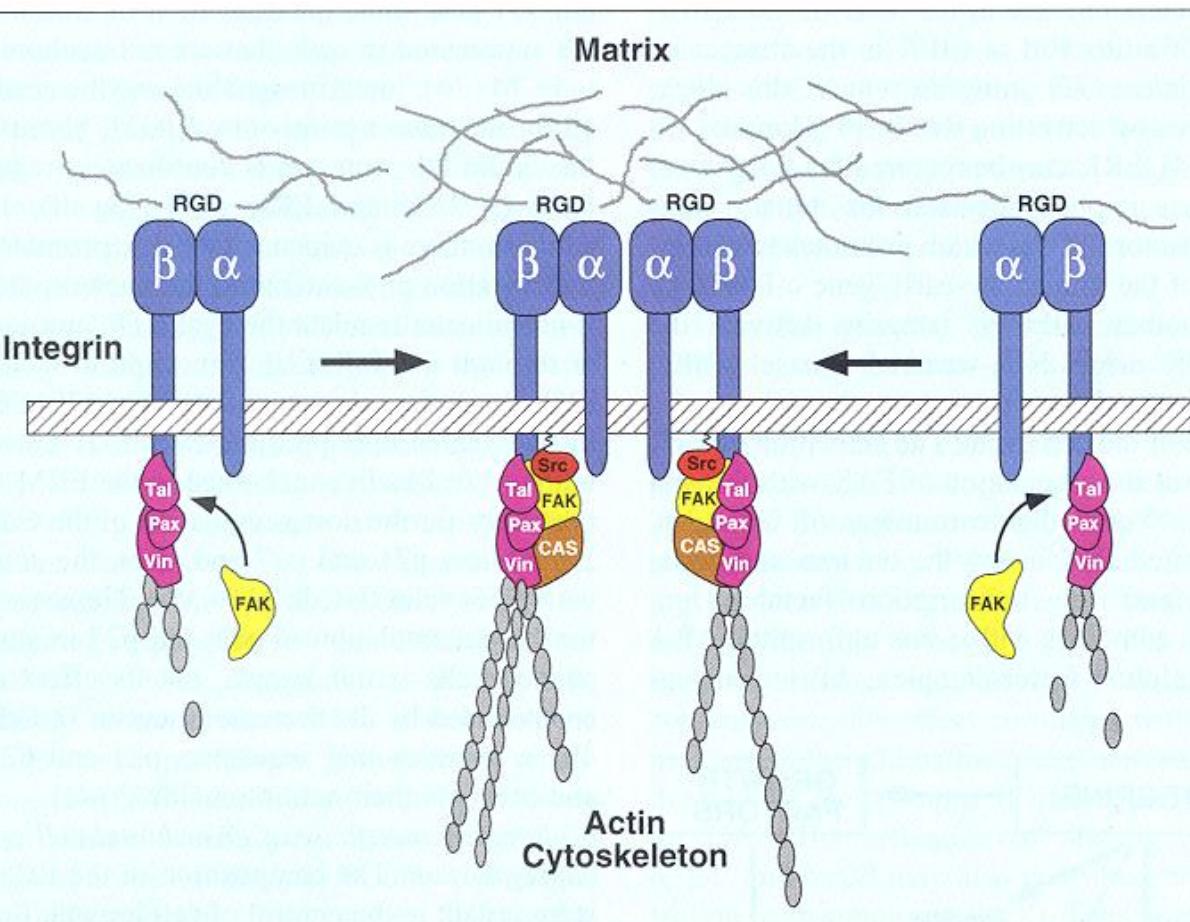
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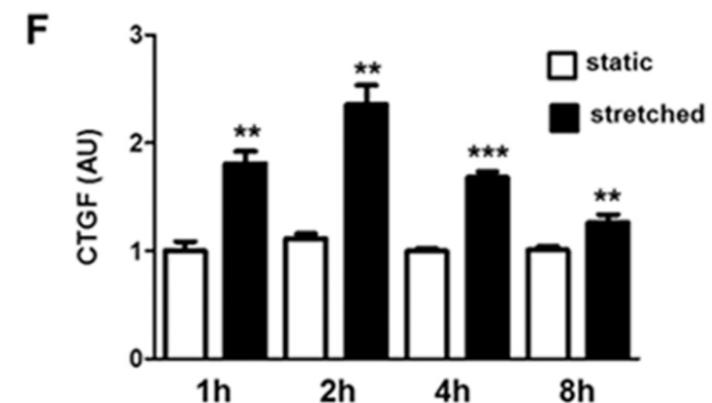
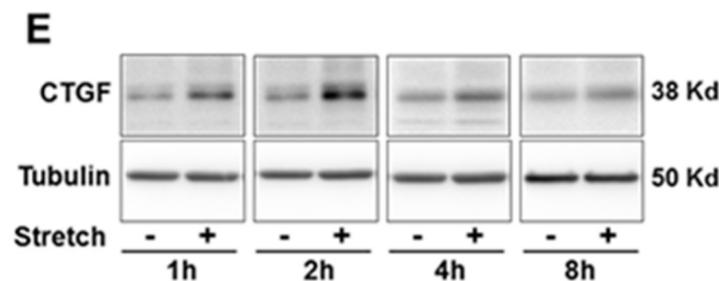
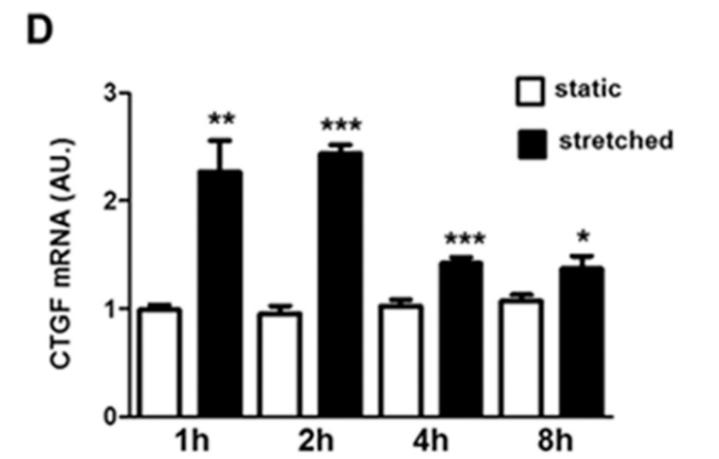
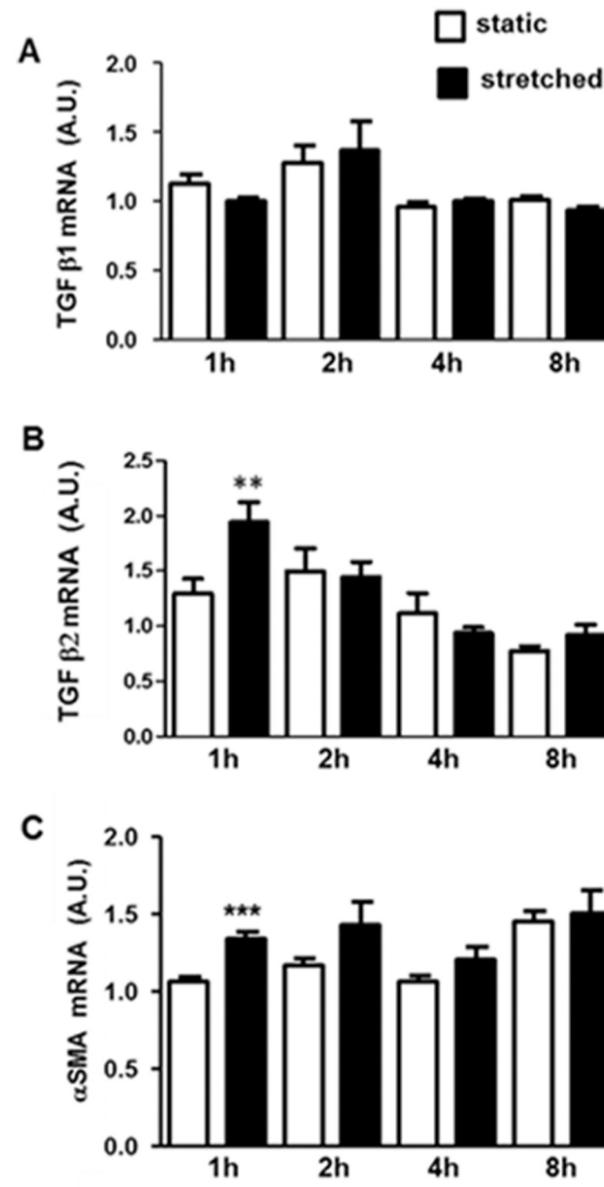


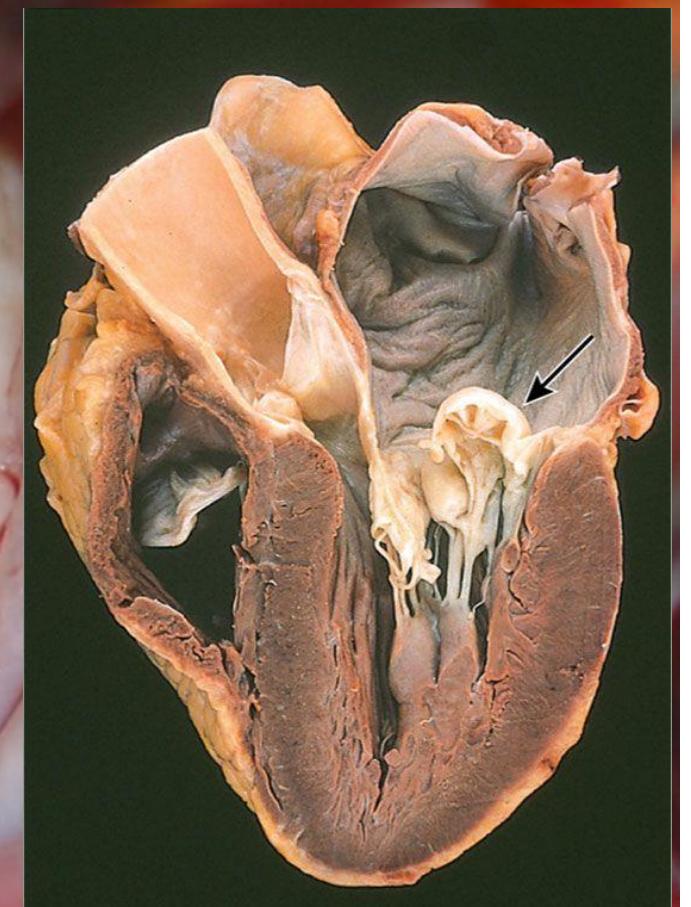
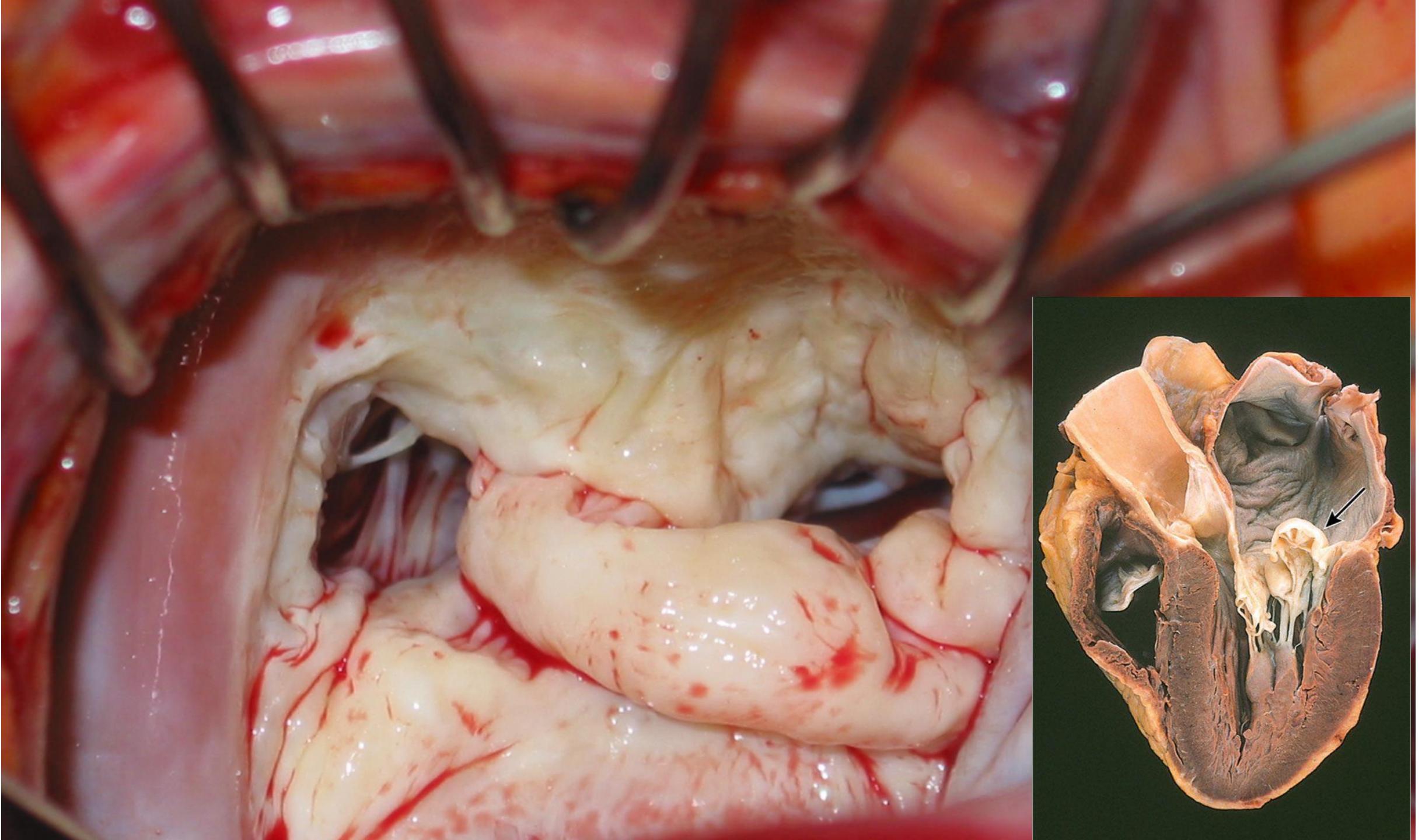
D

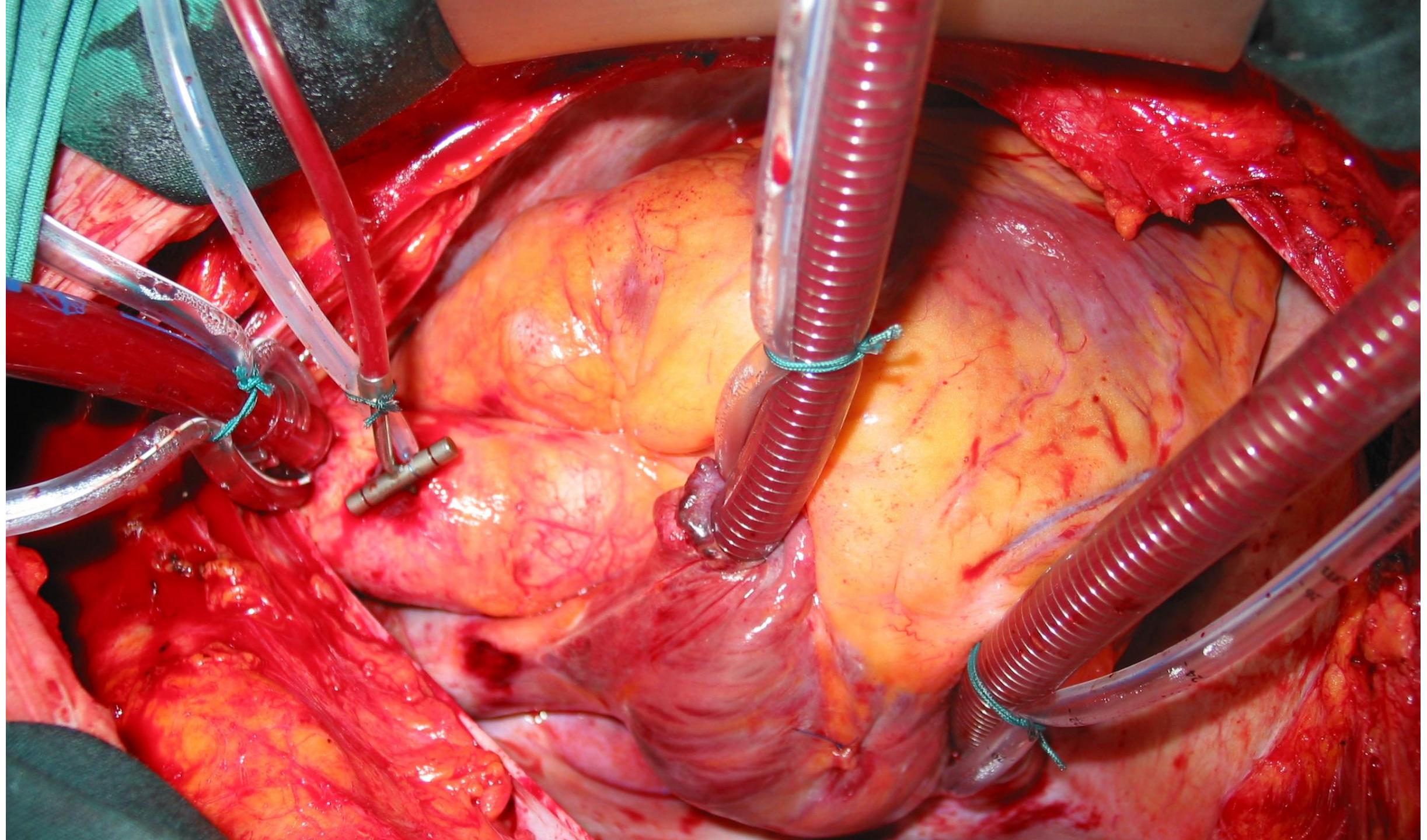


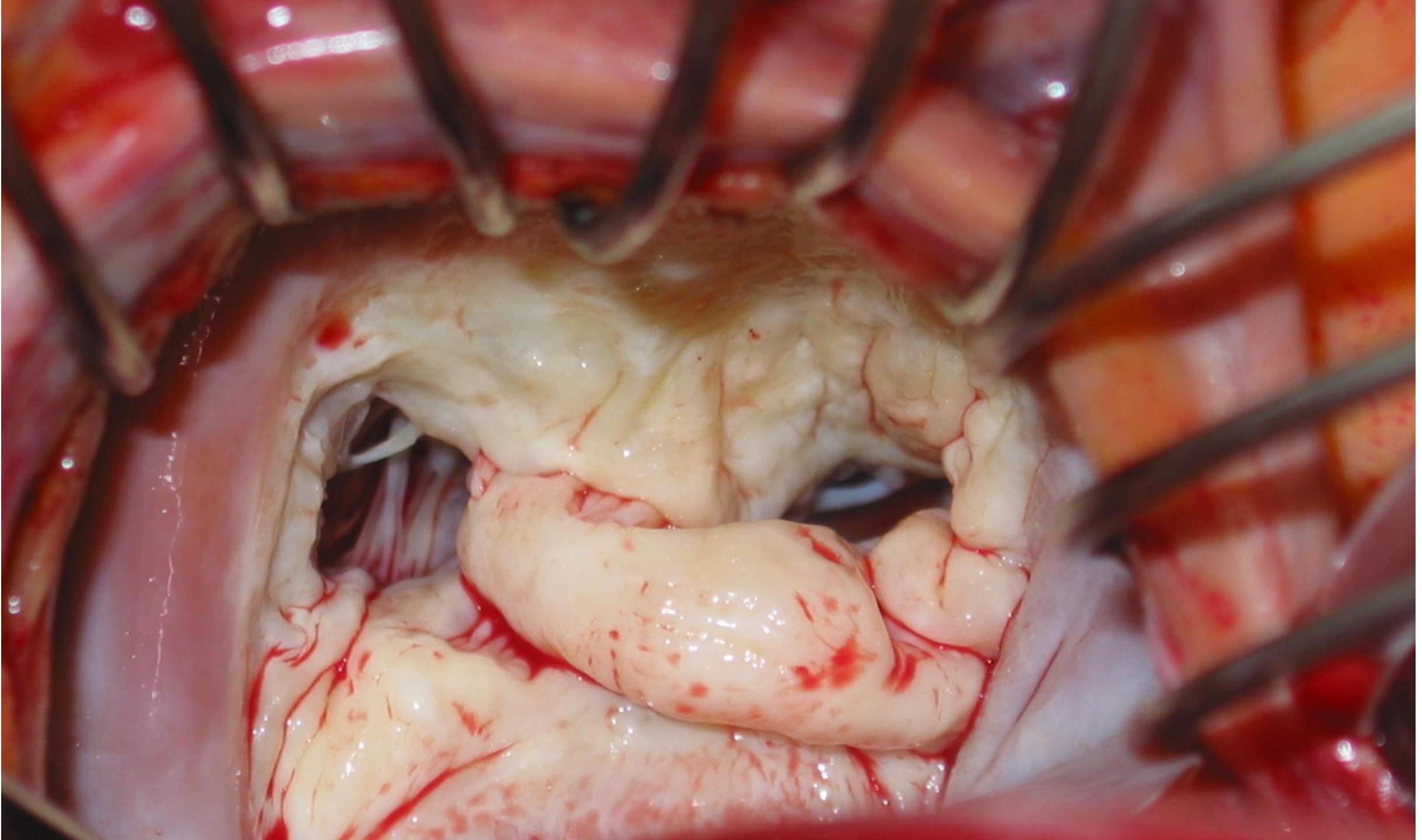
Relations matrice extracellulaire/ intégrines / FAK/ cyto-squelette d'actine

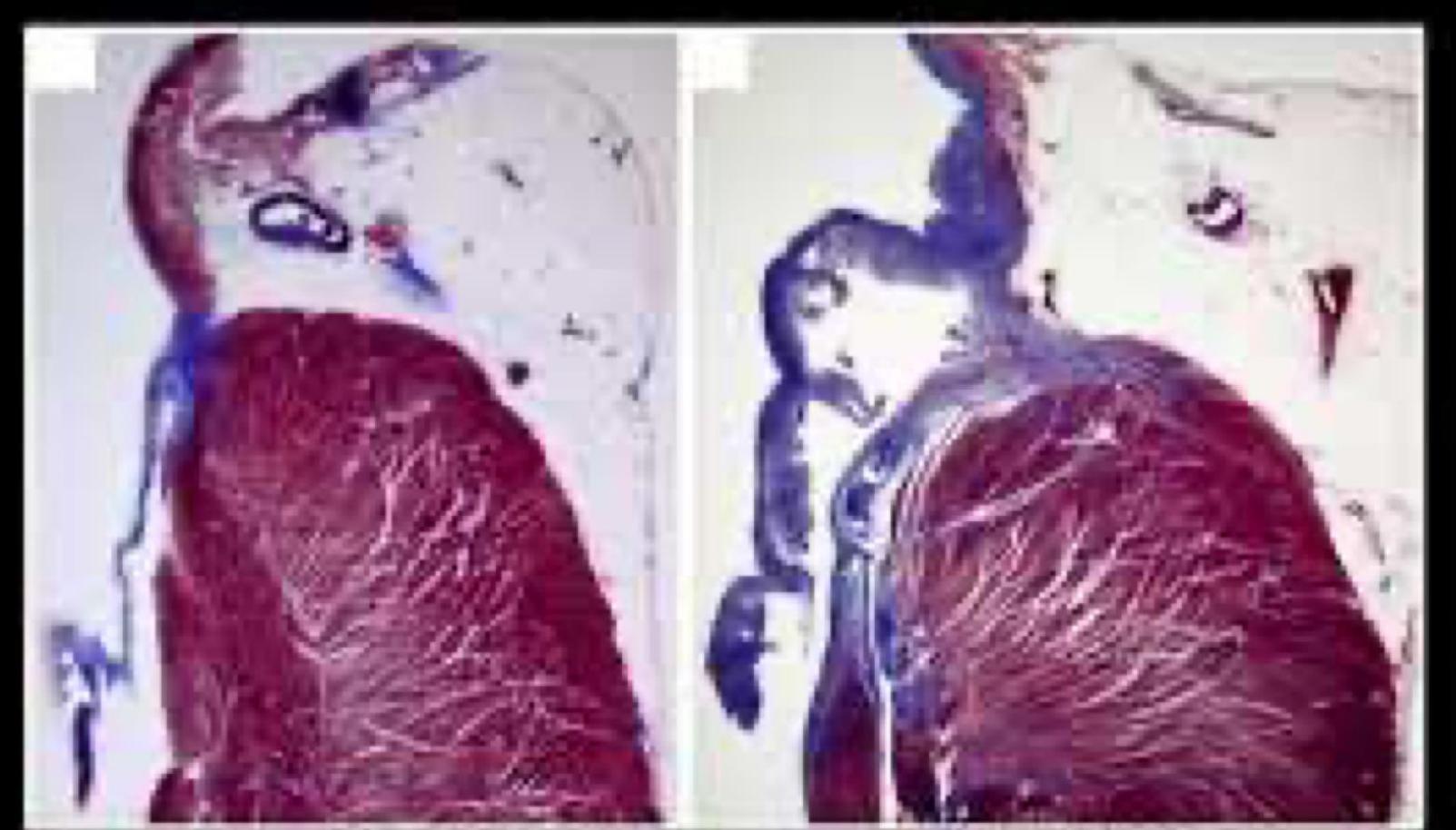






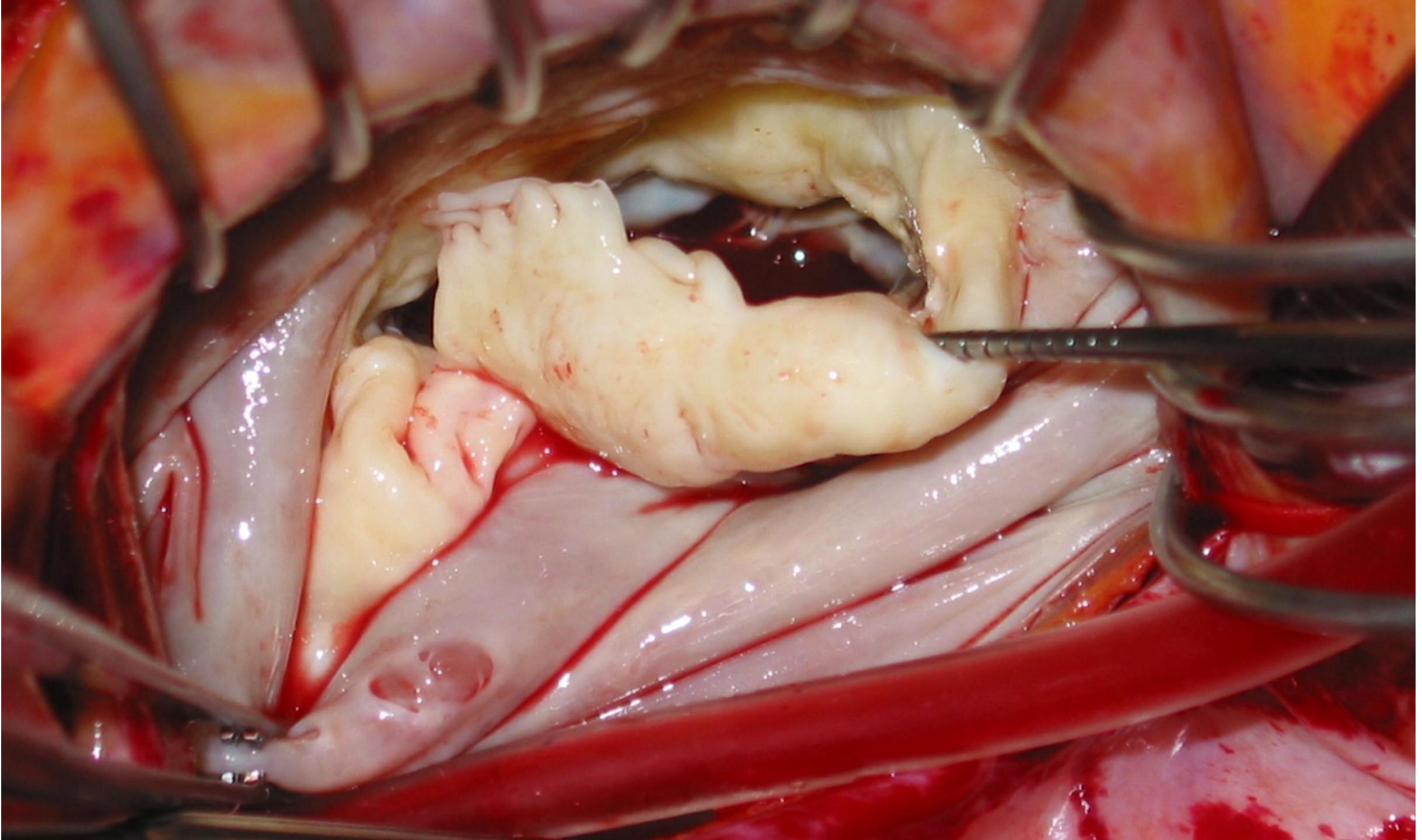


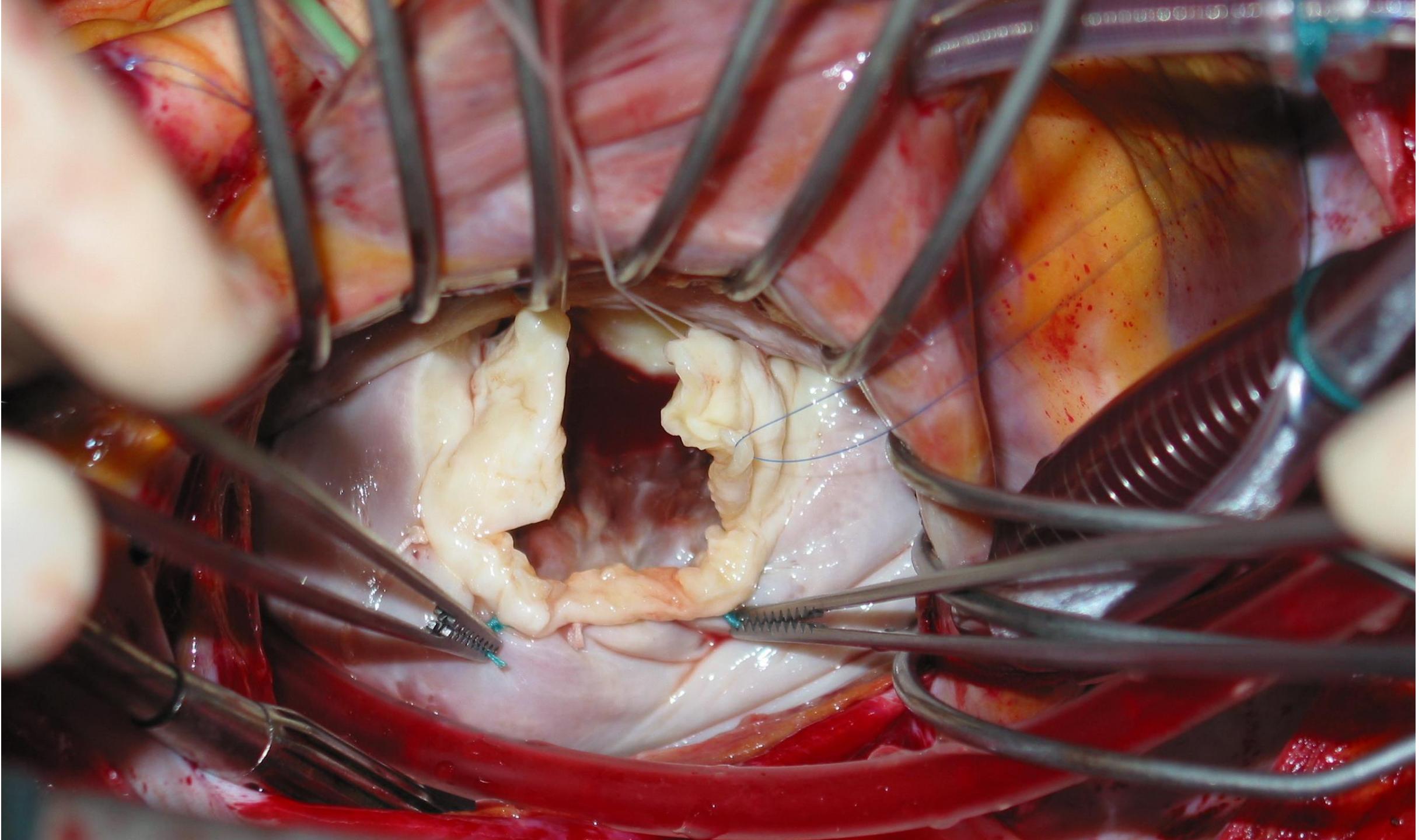


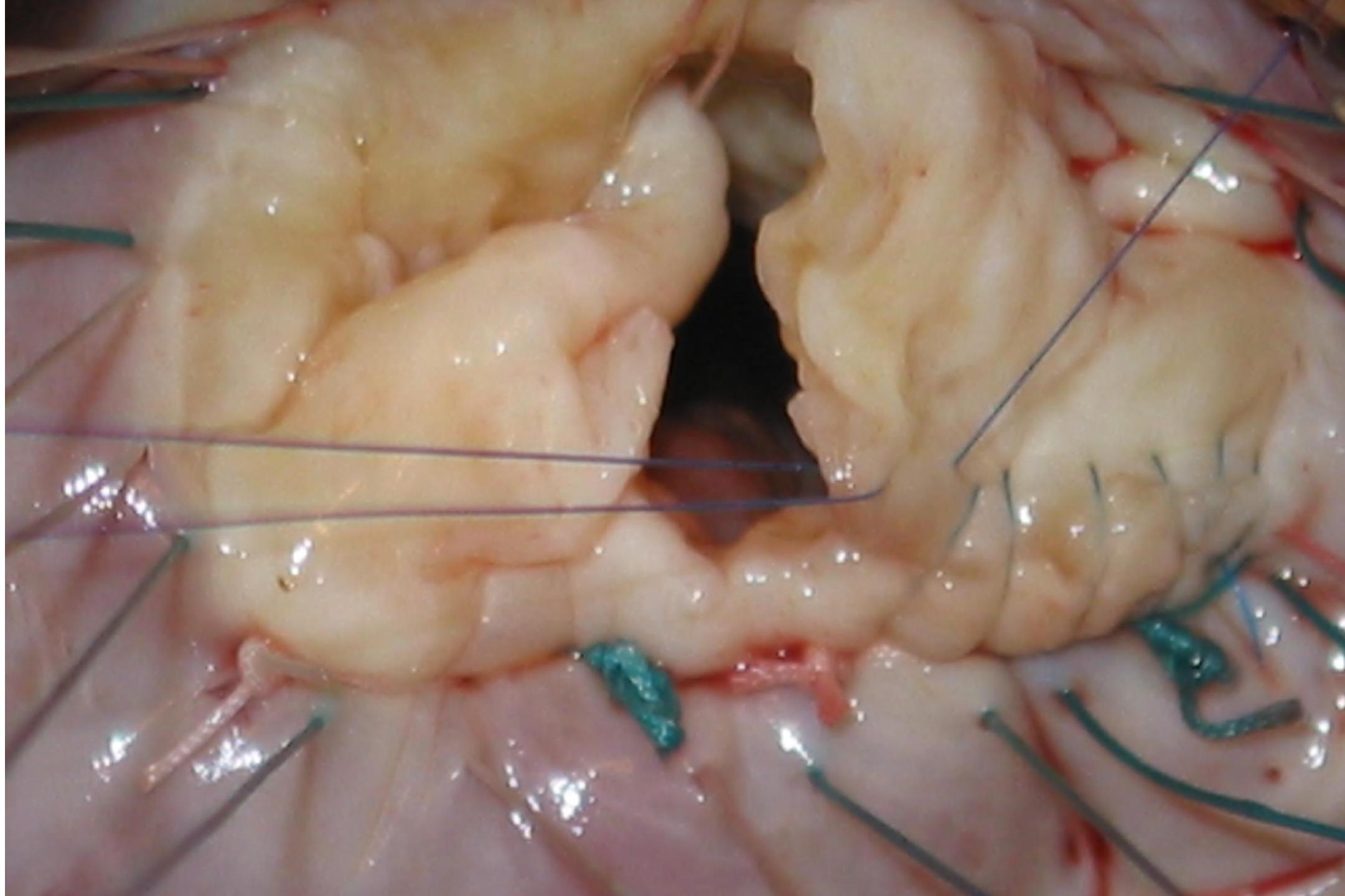


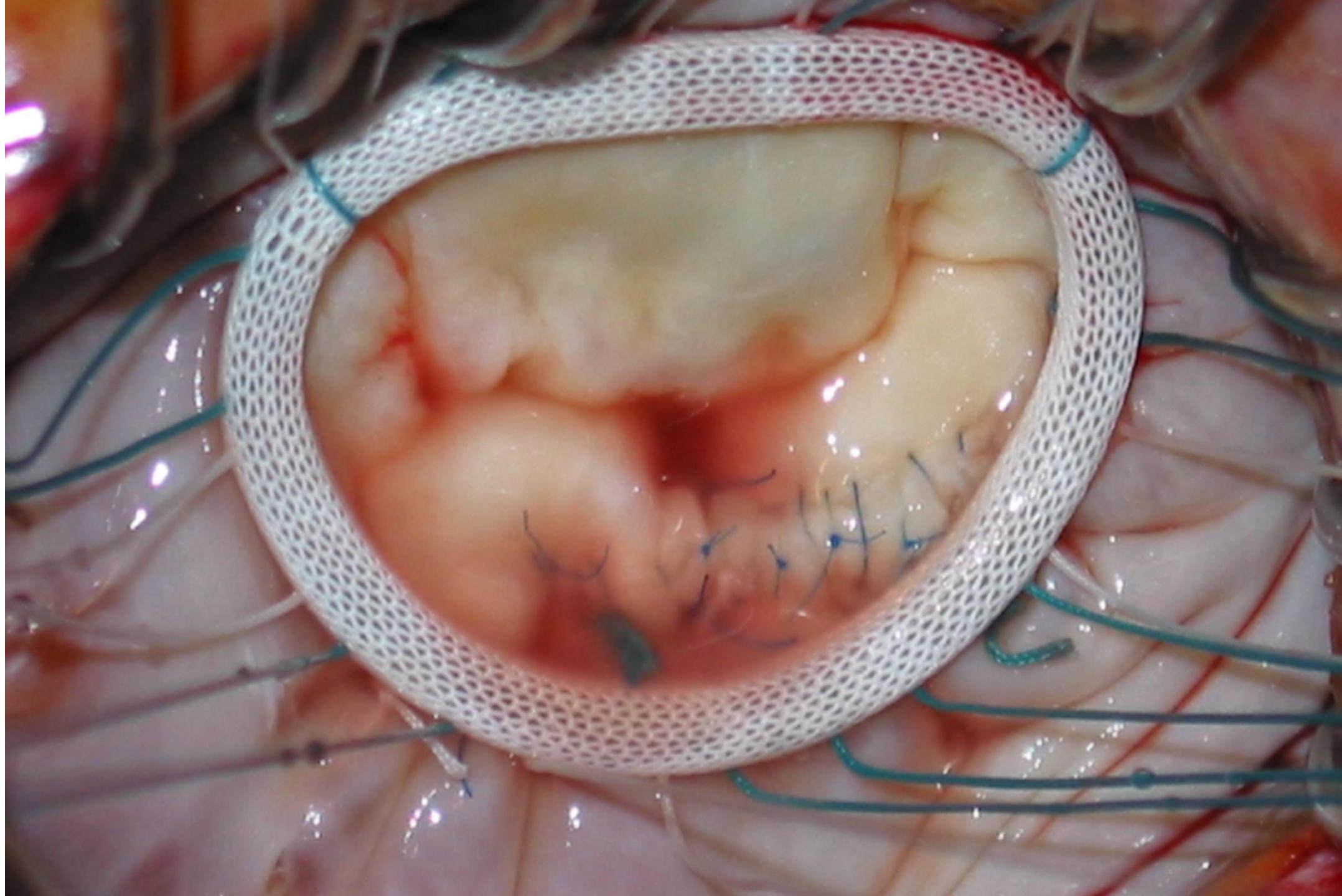
Normal Control

MVP with SCD









Chirurgie à cœur ouvert par vidéo-chirurgie et mini-thoracotomie Premier cas (valvuloplastie mitrale) opéré avec succès

First open heart operation (mitral valvuloplasty) under videosurgery through a minithoracotomy

ALAIN CARPENTIER, DIDIER LOULMET, ALEXANDRE CARPENTIER, EMMANUEL LE BRET, BÉATRICE HAUGADES,
PATRICK DASSIER, PIERRE GUIBOURT

Département de chirurgie cardio-vasculaire et de transplantation d'organes, Hôpital Broussais, 96, rue Didot, 75674 Paris Cedex 14, France

Perfusion 1998; 13: 249-252

Port-access mitral valve surgery

H Vanermen, Y Vermeulen, F Wellens, R De Geest, I Degrieck and F Van Praet Department of
Cardiovascular and Thoracic Surgery, OLV Clinic, Aalst

Chirurgie mini-invasive vidéo-assistée de la valve mitrale





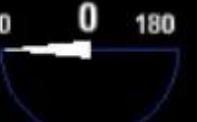
Echo adulte

TIS0.1 MI 0.4

X7-2t

53Hz

12cm



2D

53%

C 50

P Arrêt

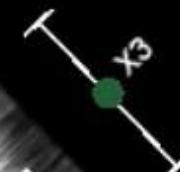
Gén

M4



PAT T: 37.0C

TEE T: 38.9C



76 bpm

Echo adulte

X7-2t

7Hz

6.3cm

Zoom 3D

2D / 3D

% 50 / 44

C 50 / 30

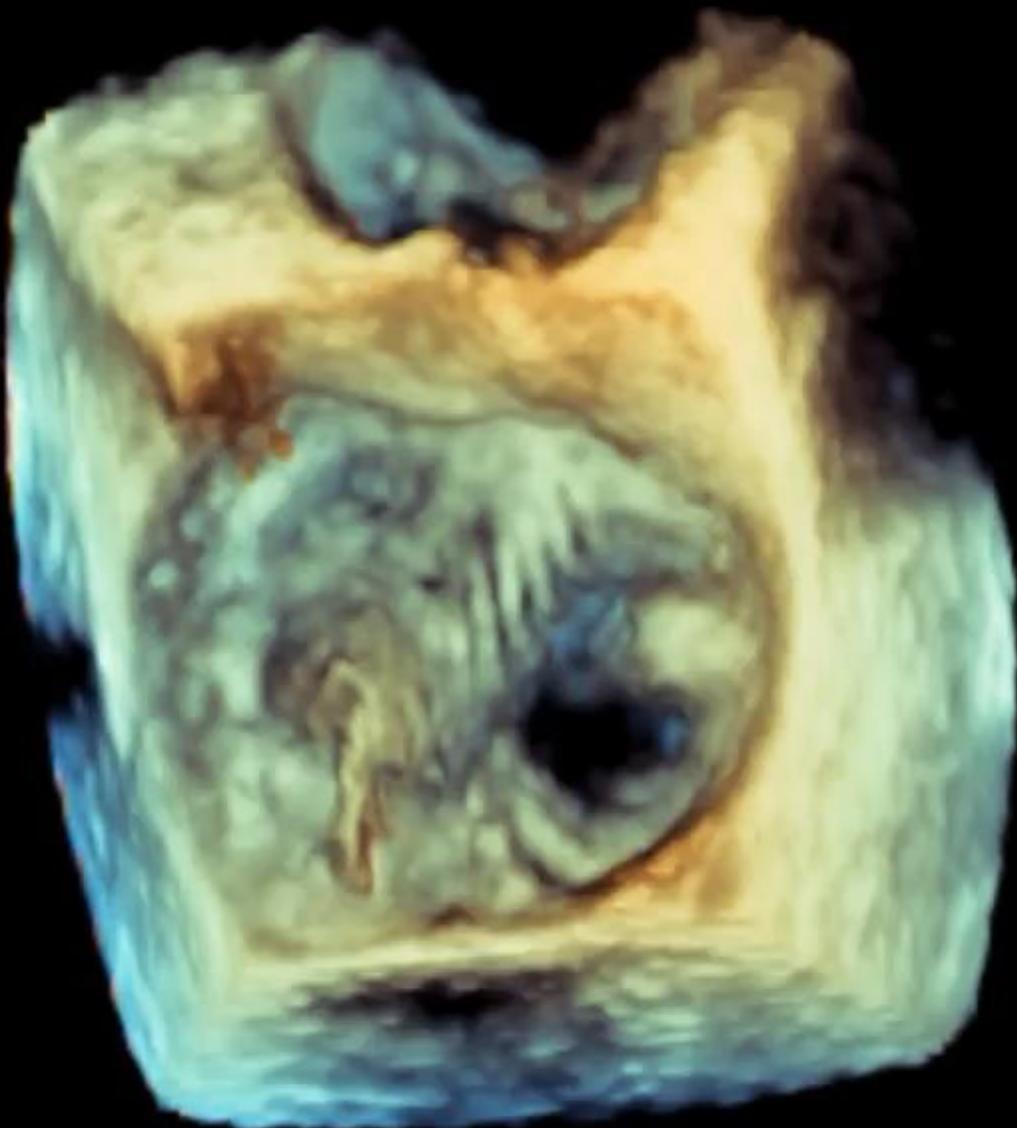
Gén



Battem. 3D 1

TIS0.1 MI 0.3

M4

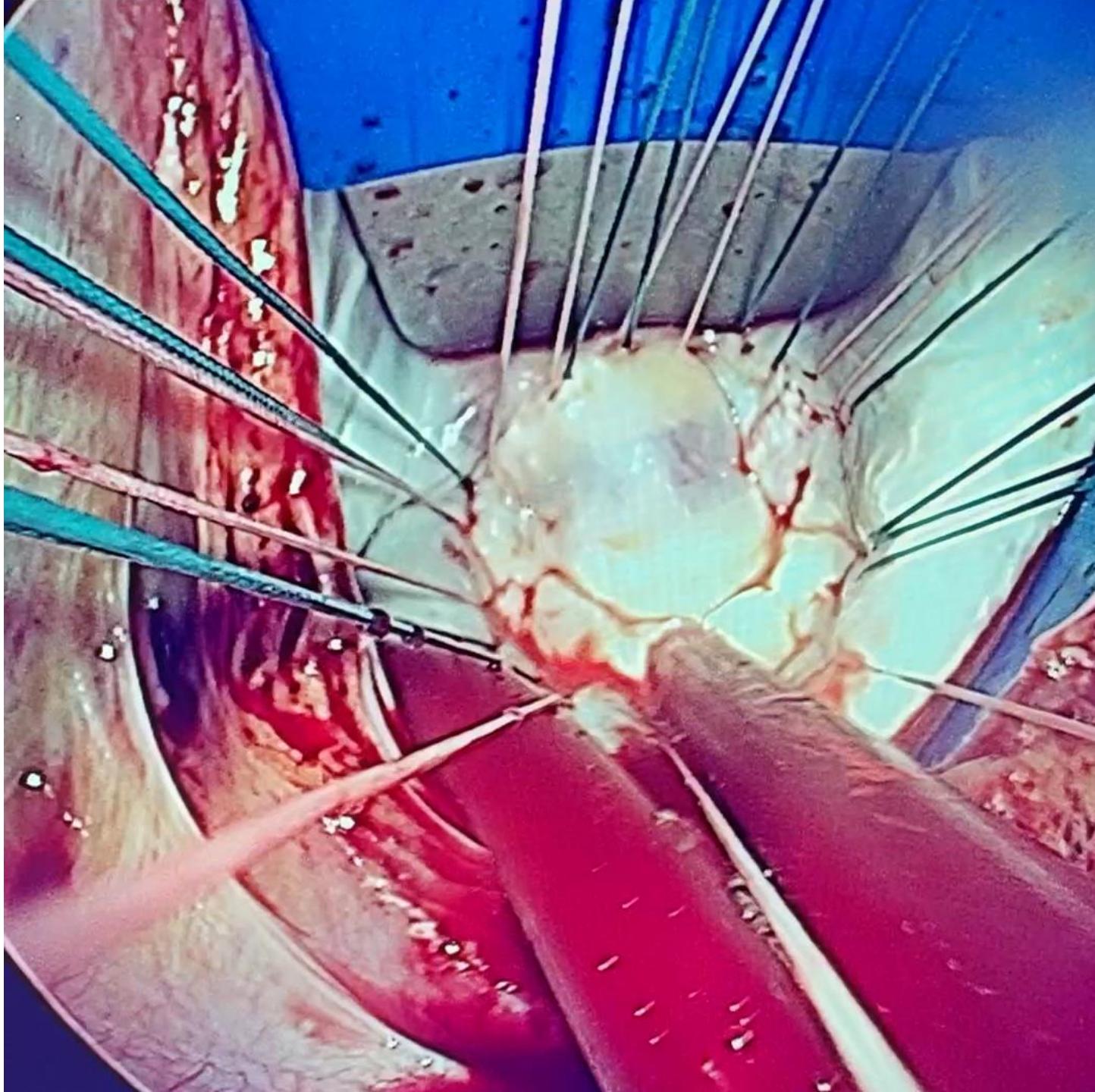


PAT T: 37.0C

TEE T: 40.6C



76 bpm



Echo adulte

TIS0.6 MI 0.3

X7-2t

17Hz

12cm

2D

57%

C 50

P Arrêt

Gén

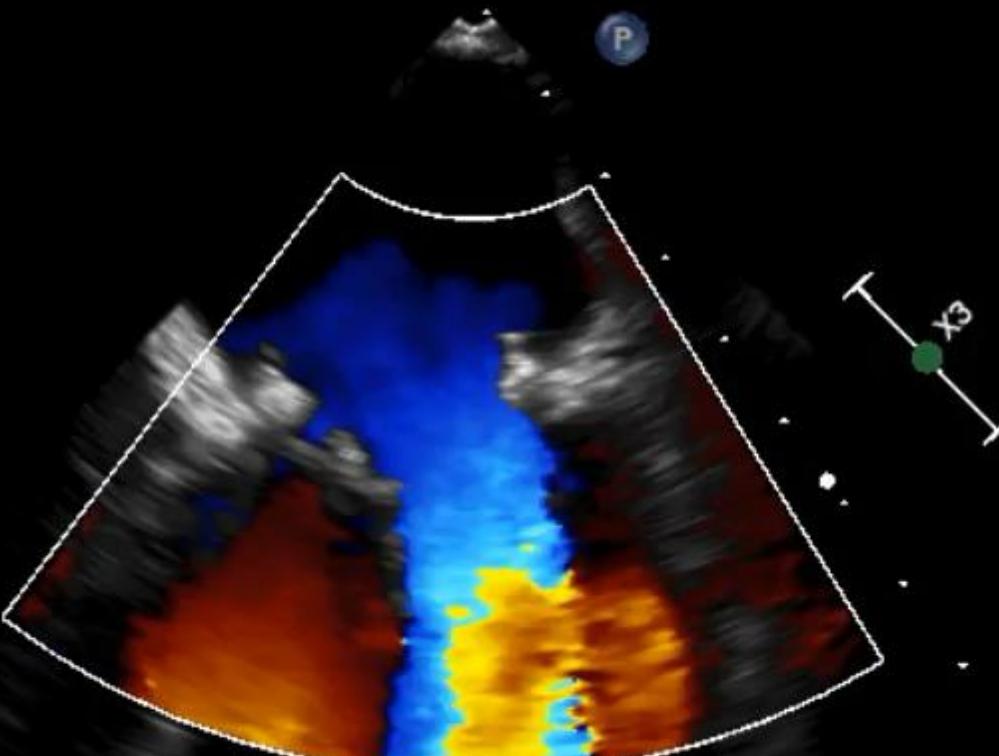
Coul

48%

6838Hz

FP 615Hz

4.4MHz



PAT T: 37.0C

TEE T: 39.7C



87 bpm

Echo adulte

X7-2t

6Hz

6.5cm

Zoom 3D

2D / 3D

% 52 / 44

C 50 / 30

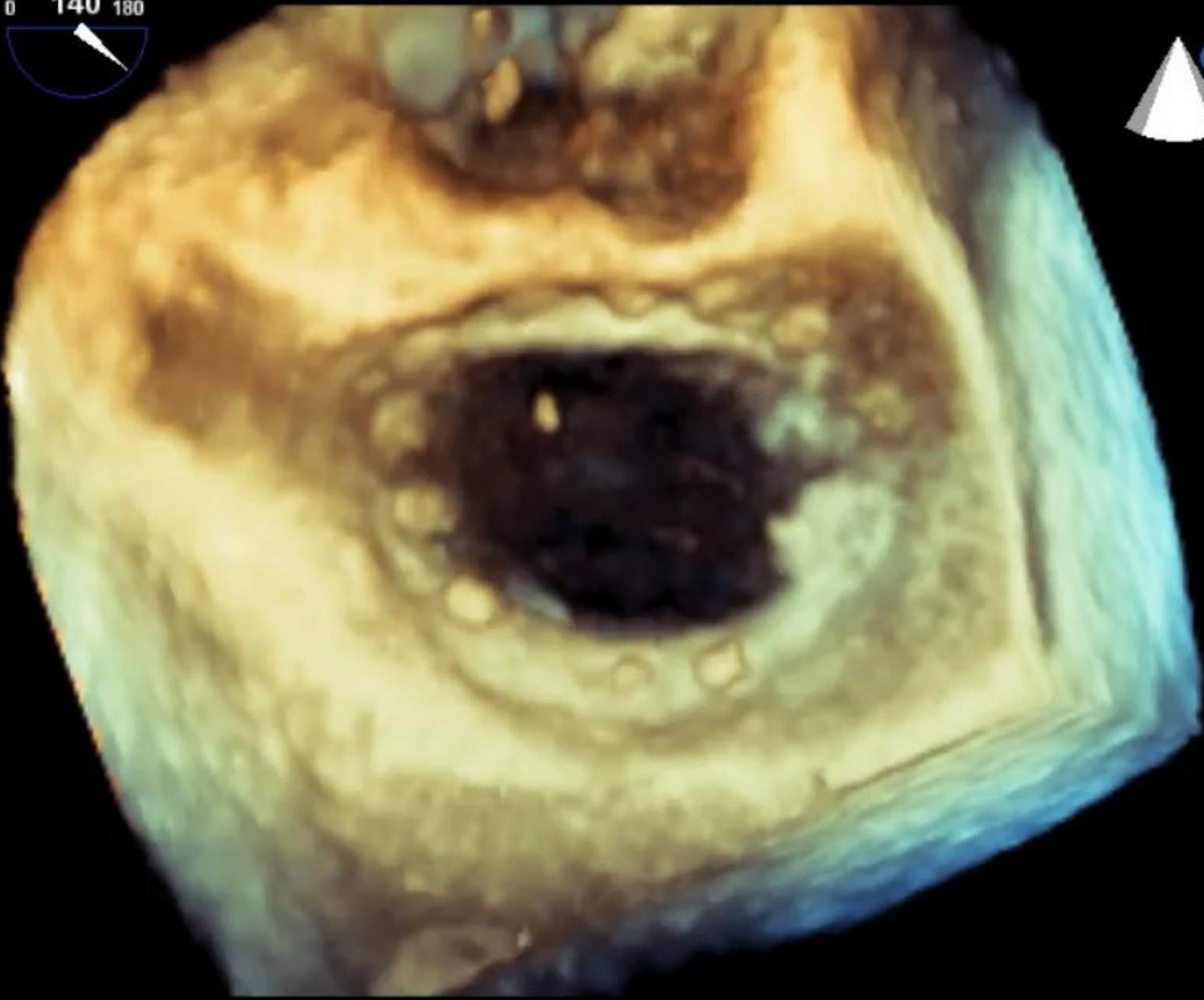
Gén



Battem. 3D 1

TIS0.1 MI 0.3

M4

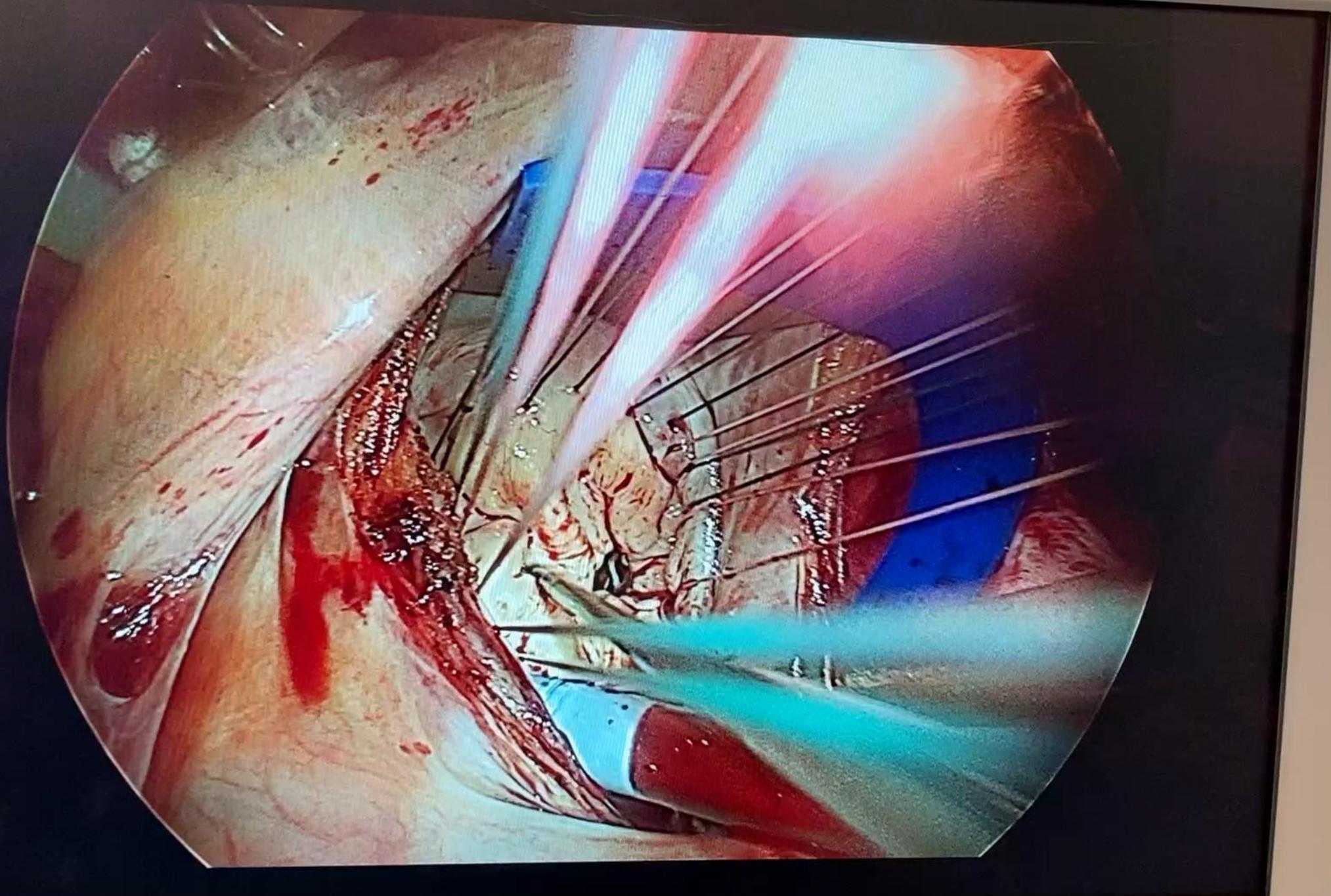


PAT T: 37.0C

TEE T: 40.2C

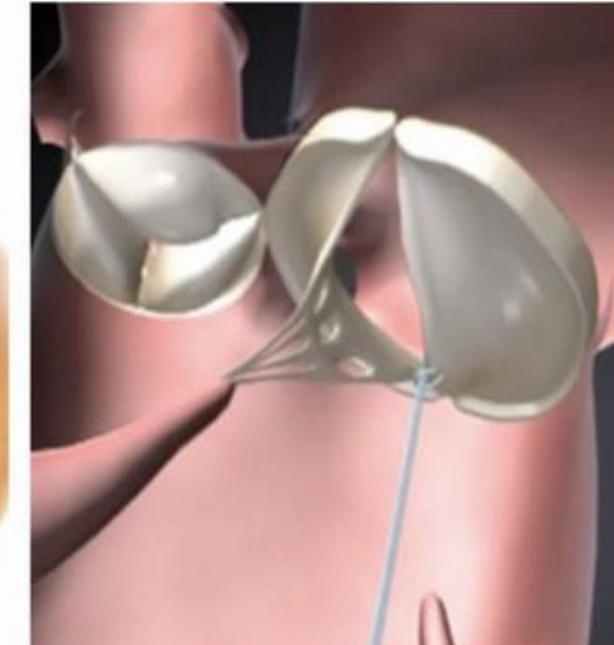


78 bpm

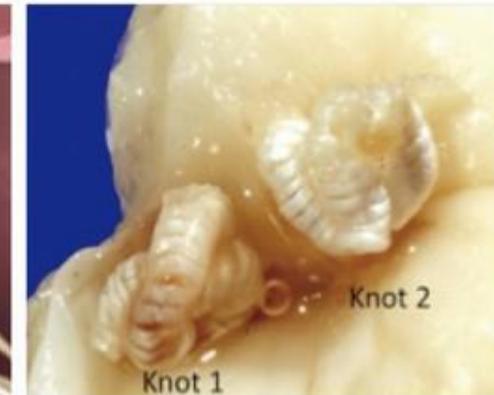
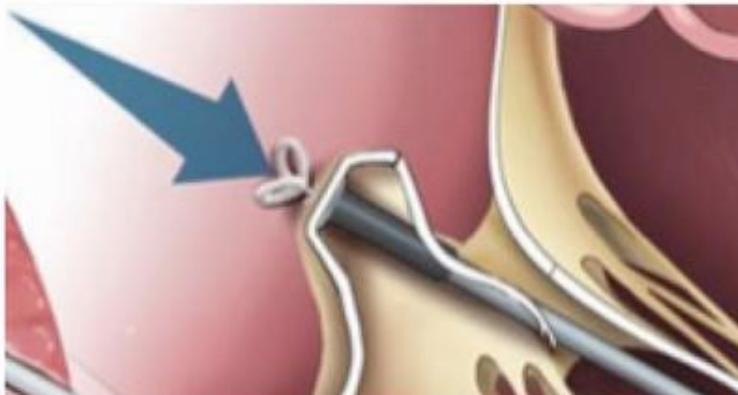
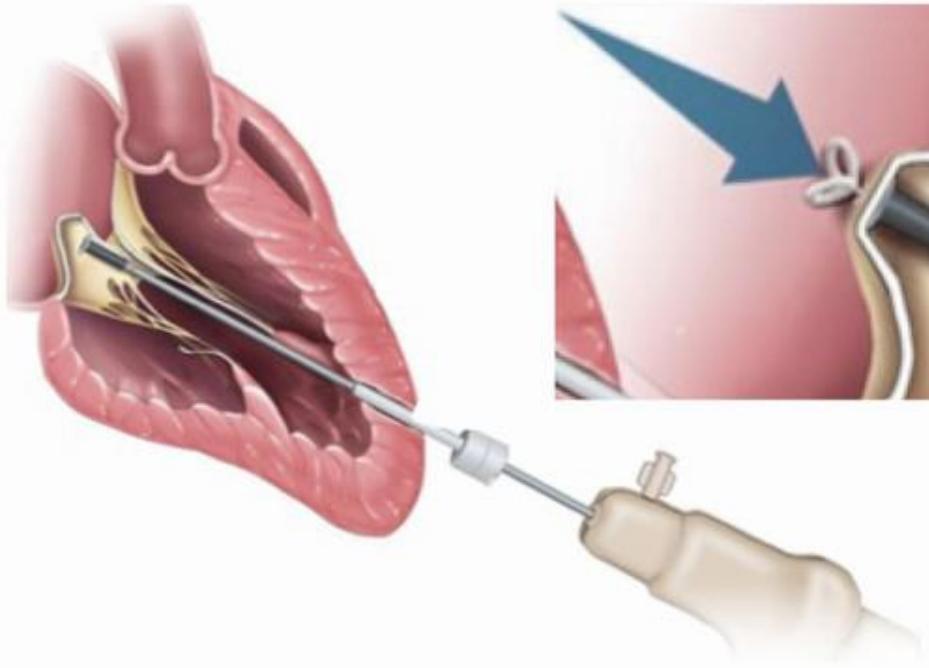


0

A



B



Transapical beating-heart chordae implantation in mitral regurgitation: a new horizon for repairing mitral valve prolapse

Patrizio Lancellotti^{1,2}, Marc Radermecker^{3,4}, Rodolphe Durieux³, Thomas Modine⁵, Cécile Oury¹, Khalil Fattouch^{6,7}

Conclusions 1

Le complexe valvulaire mitrale est une structure dynamique ; les cellules **VICs** jouent un rôle déterminant dans le **remodelage myxoïde** du tissu , processus peut-être adaptatif initialement mais qui annonce la **dysfonction valvulaire** et la pathologie cardiaque (IM)

Le LBTC/GIGA ont pu démontrer le rôle des **MT1/2** (Stress oxydatif) et d'autre part le rôle des **contraintes mécaniques** dans **l'activation des VICs** et l'initiation du **remodelage myxoïde**

Le développement **d'inhibiteurs pharmacologiques** permet d'envisager le contrôle medical du remodelage valvulaire

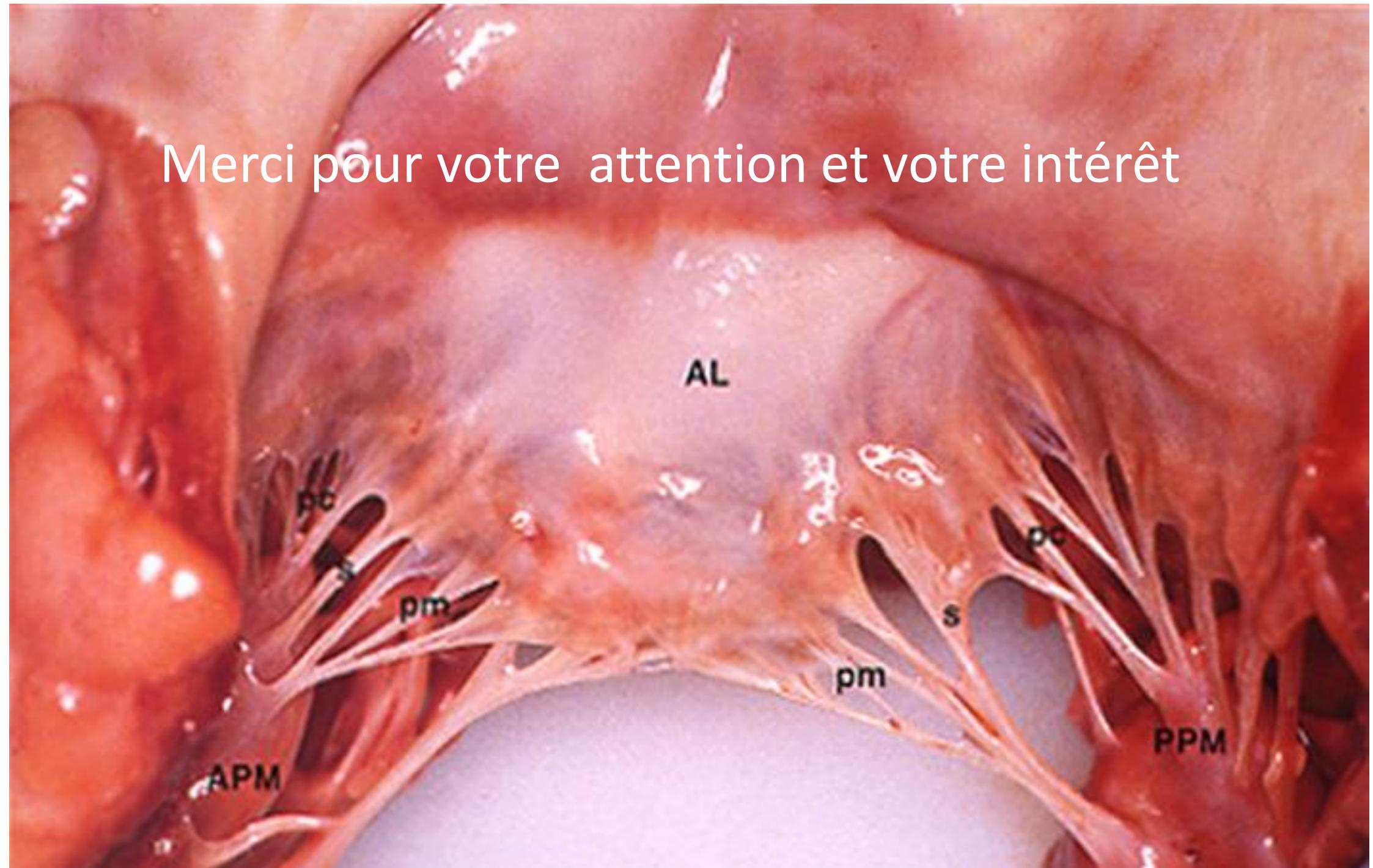
Conclusion 2

- La chirurgie réparatrice s'appuie toujours sur les principes énoncés par Carpentier dans les années 80.
- La réparation reste l'option de choix et est une opération durable

Conclusion 3

- La plastie mitrale a été à la base du développement de la chirurgie “mini-invasive”
- Opération efficace et durable, elle voit sa **valeur** augmenter par une approche plus respectueuse des tissus
- **Valeur = “efficacité”/ “invasivité”**

Merci pour votre attention et votre intérêt



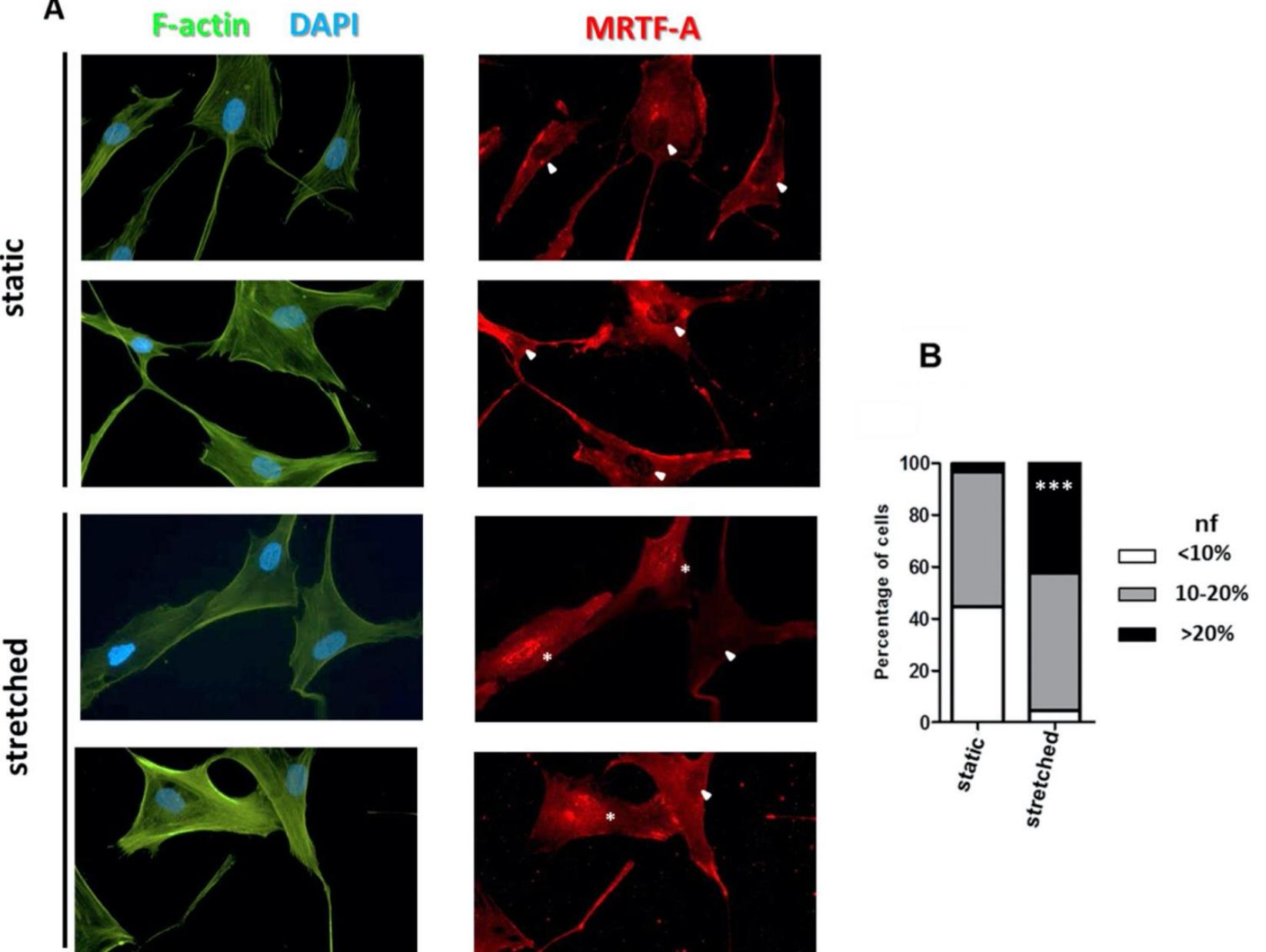
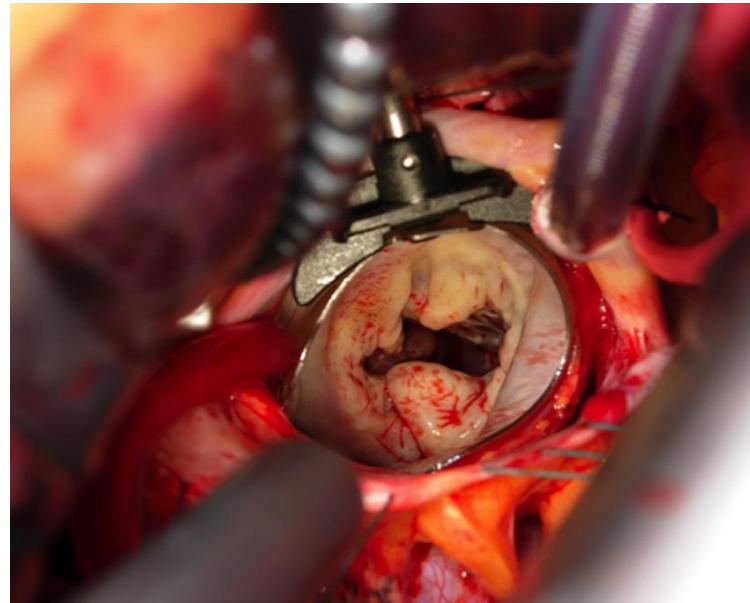
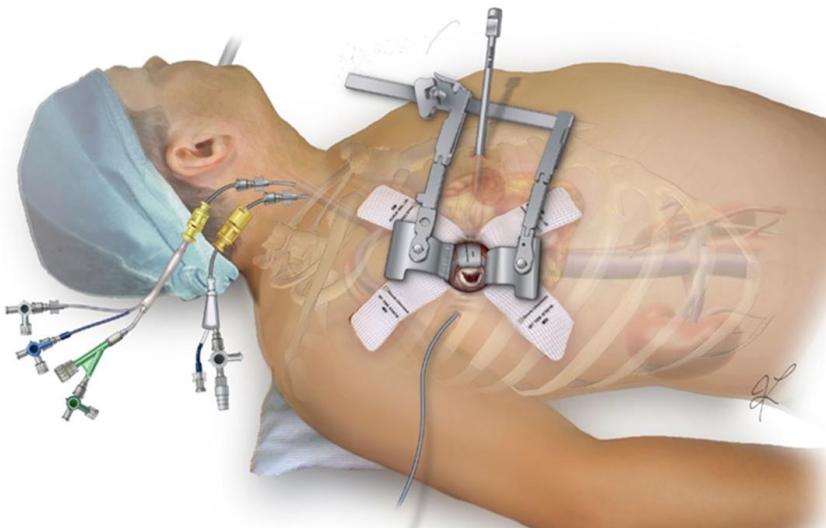
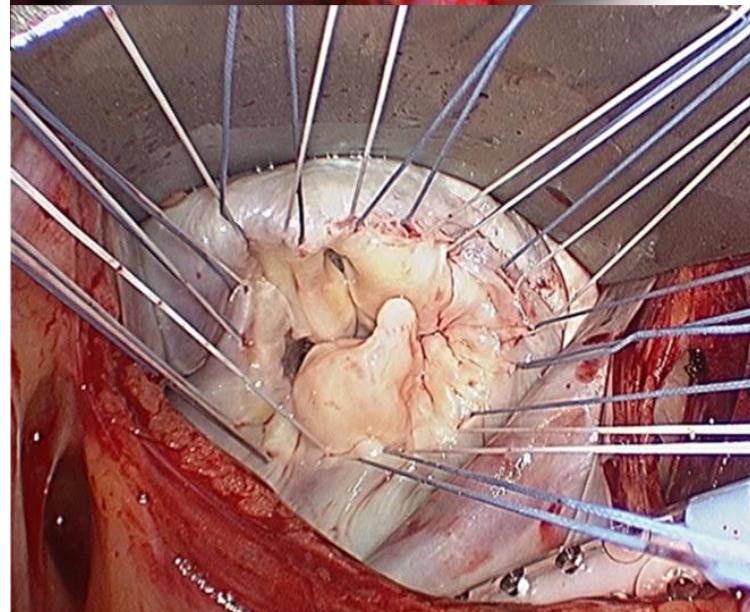


Fig. 4. Cyclic-stretch induces MRTF-A nuclear translocation. Representative staining of actin fibers by FITC-phalloidin (green), nuclei by DAPI (blue) (left panel), and immune staining of MRTF-A (red, right panel) in static and stretched VIC for 30 min. Nuclei with a low MRTF-A fluorescence are pointed by an arrowhead and those with a strong MRTF-A fluorescence by an asterisk (A). Distribution of cells (in %) according to the nuclear fluorescence (nf) staining for MRTF-A relative to the total fluorescence of the cell (%) measured on 58 (static) and 45 (stretched) cells in 4 separate experiments (**p < .001) (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

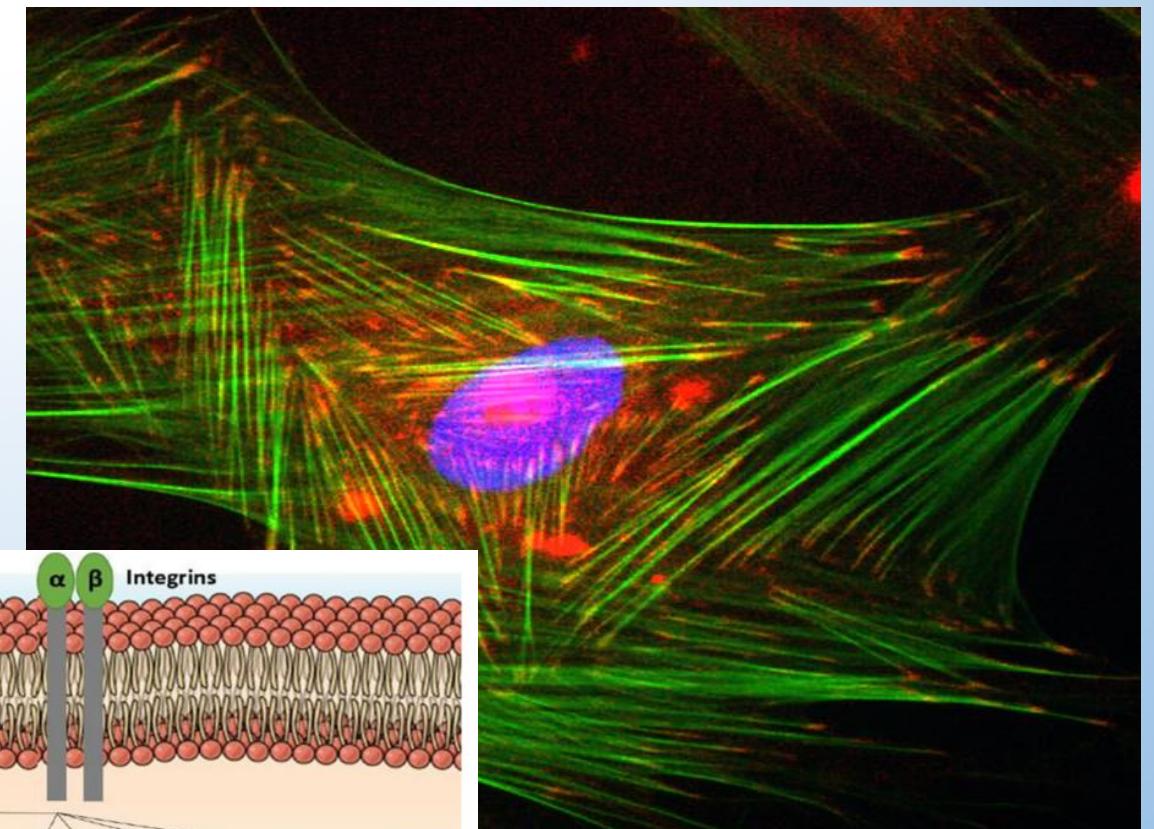
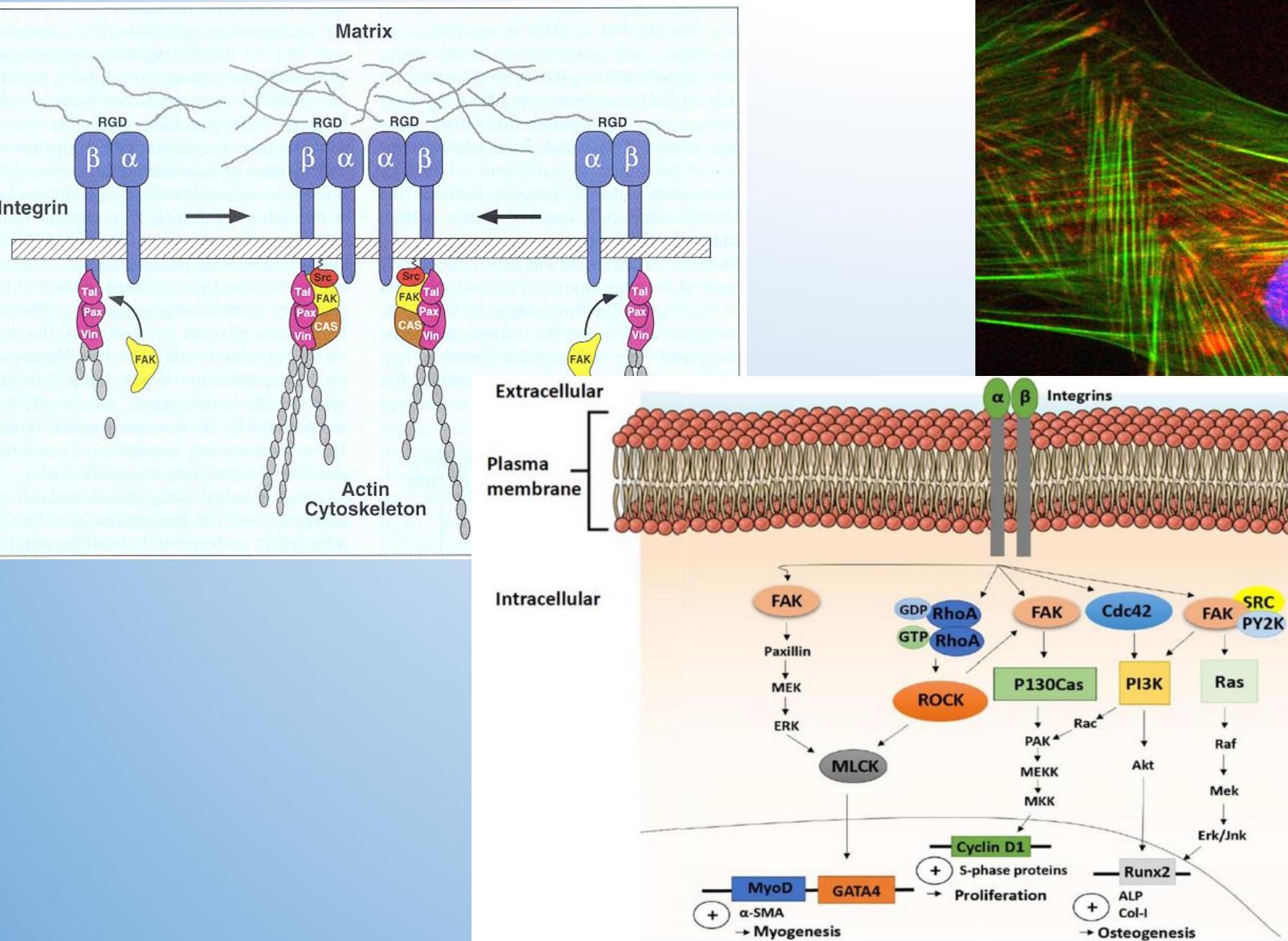
Video Assisted Mitral Valve Surgery



- Canulation artérielle et veineuse fémorales
- Décubitus dorsal
- Minithoraco droite 4^e EIC
- Vision endoscopique
- Cardioplégie antérograde
- Clampage aortique



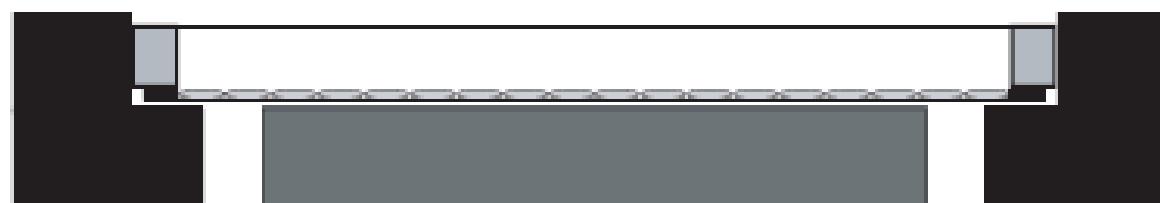
Relations matrice extracellulaire/ intégrines / FAK/ cyto-squelette d'actine



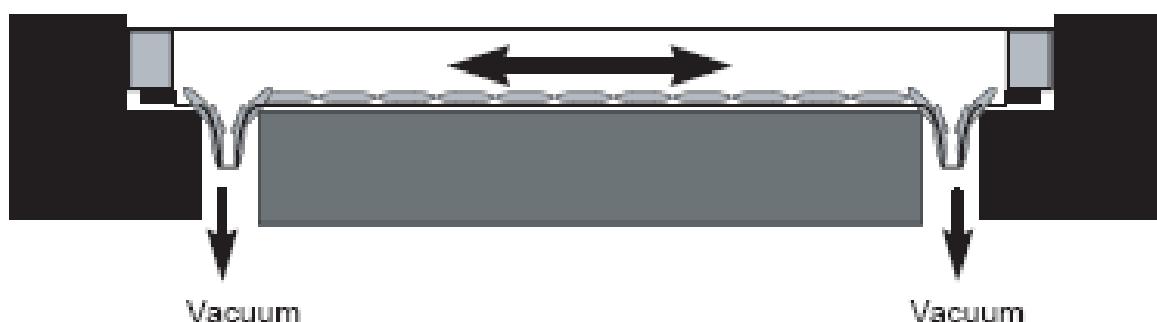
Le « stress » mécanique stimule RhoC, mais non RhoA ou Rac1, ce qui induit la voie Rock1-2 et la formation de fibres d'actine à partir d'actine globulaire monomérique. Et ceci a été montré par utilisation d'inhibiteurs spécifiques (Animation 1 puis A2). Puisque l'actine globulaire monomérique est utilisée pour former les fibres (A3), sa concentration cytoplasmique diminue, ce qui entraîne la dissociation du complexe MRTF-A-gActine. (A4) Une seconde voie de régulation est induite par le stress mécanique, qui, in fine, va induire la phosphorylation de Erk et du MRTF-A cytoplasmique. (A5) Celui-ci va alors pénétrer dans le noyau, s'associer à SRF, et induire la synthèse de facteurs qui vont favoriser l'activation des VICs et le remodelage du tissu valvulaire



Valvular interstitial cells



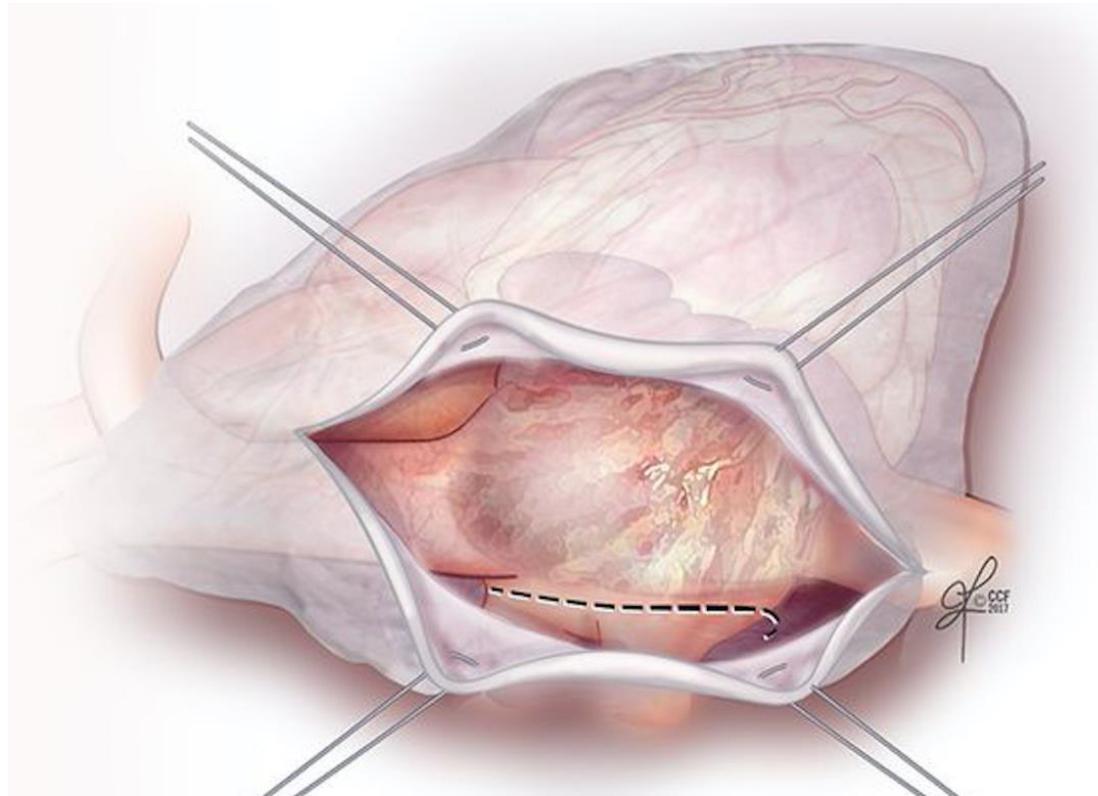
Groove



Vacuum

Vacuum

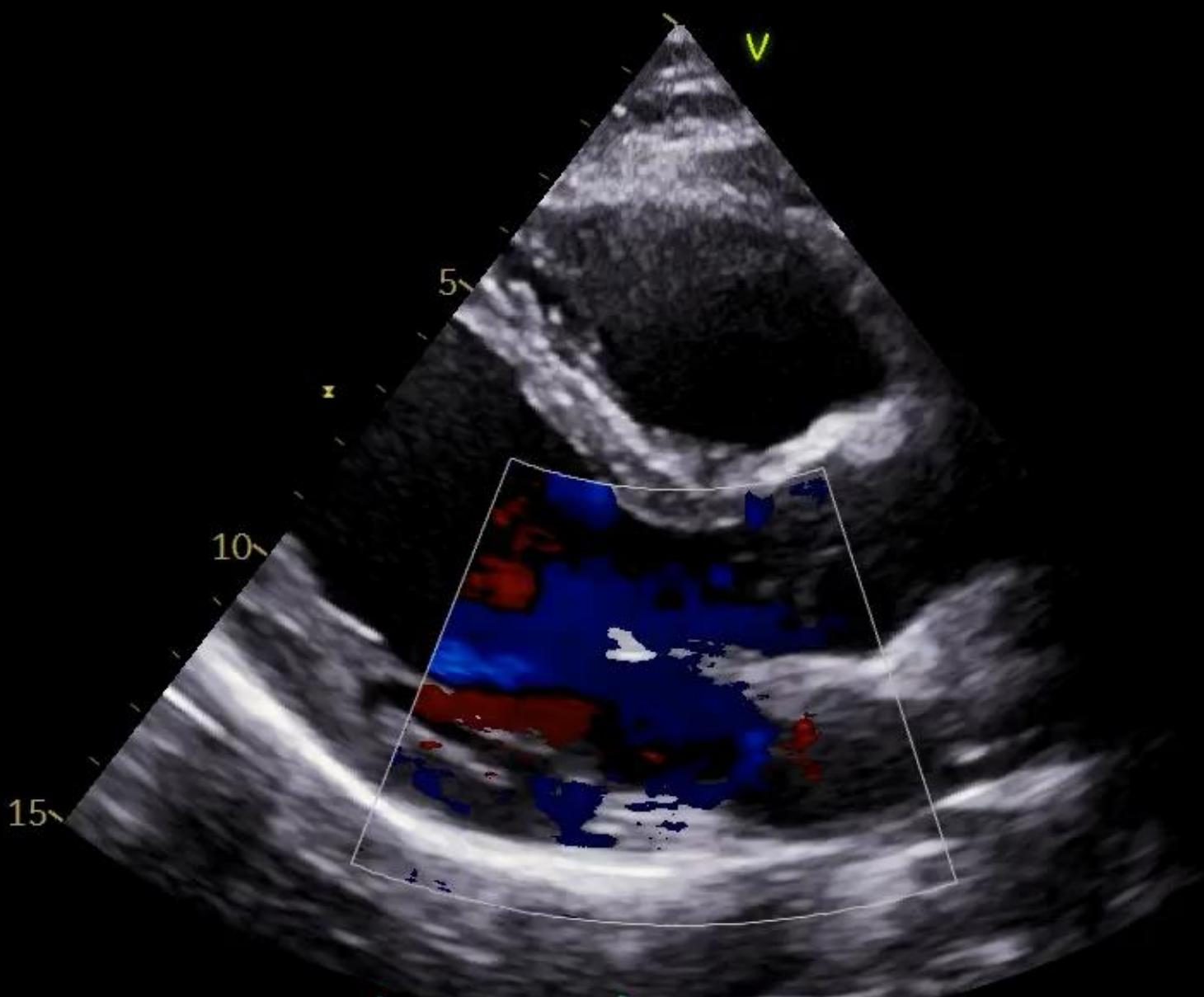
Chirurgie mini-invasive vidéo-assistée de la valve mitrale



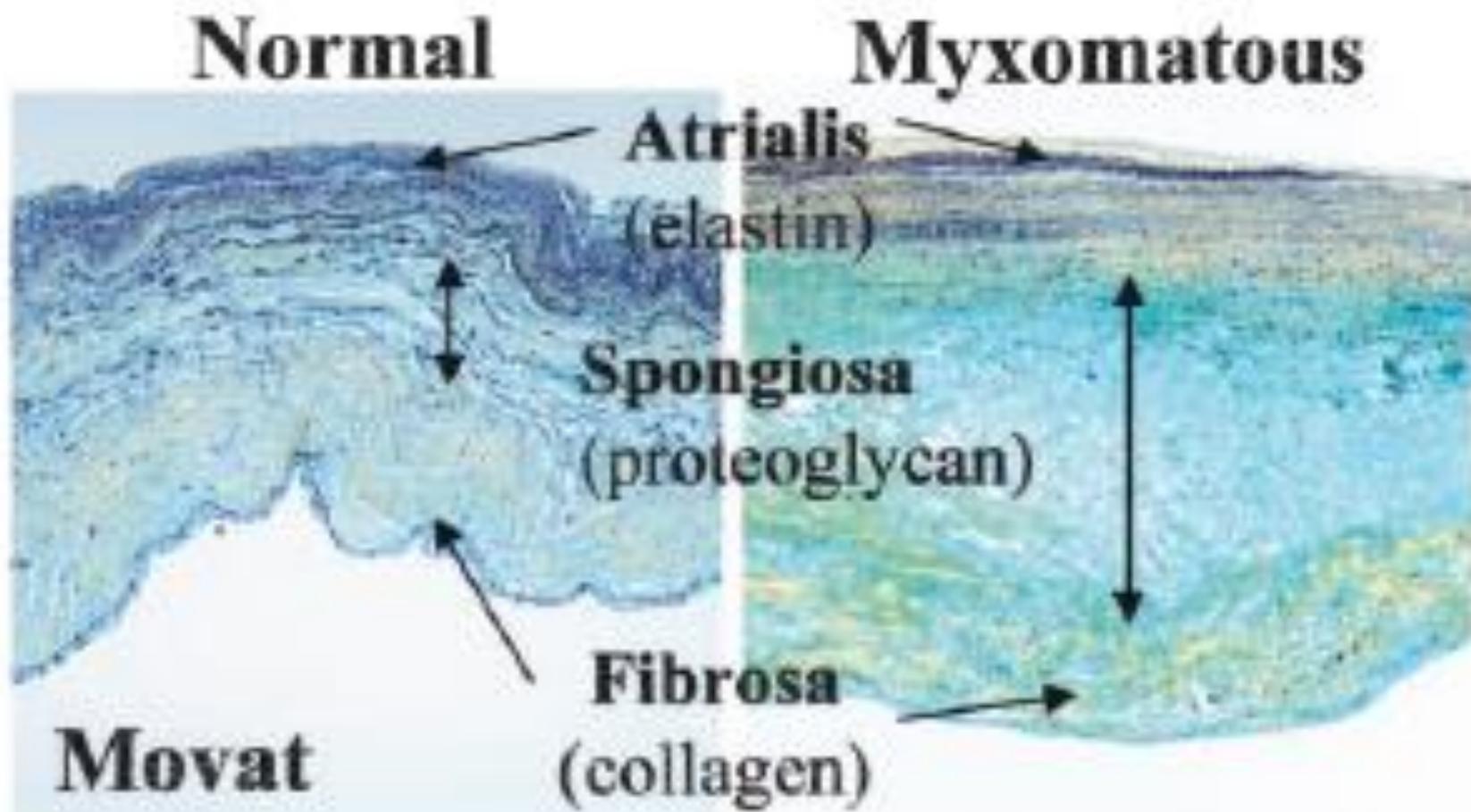
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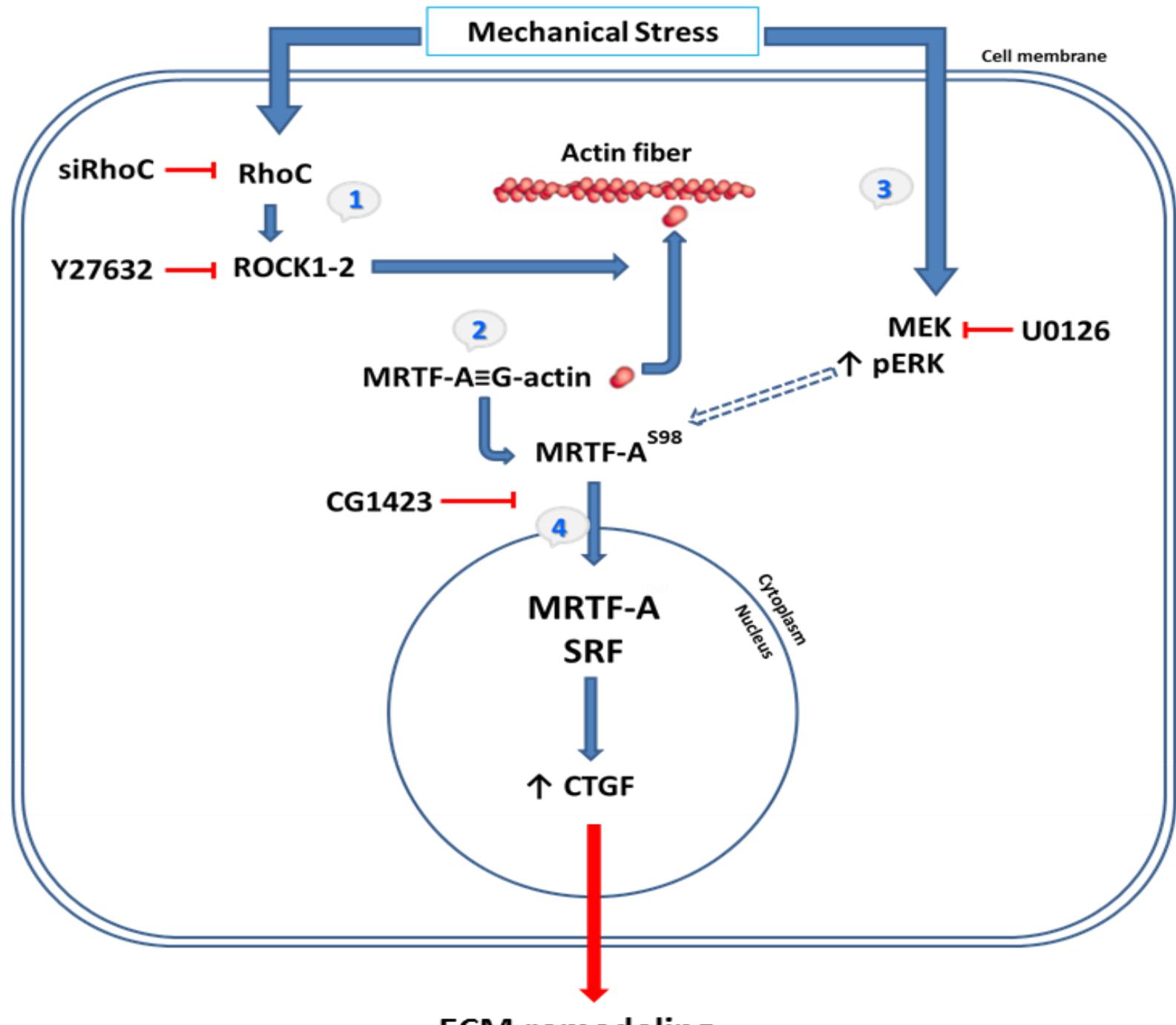
.65

-.65



92
2:44HR





Genetic susceptibility
and/or
Acquired defect



MT1/2



TGF- β 2



Activated
VIC → Versican
accumulation ← ADAMTS
repression

ECM remodelling

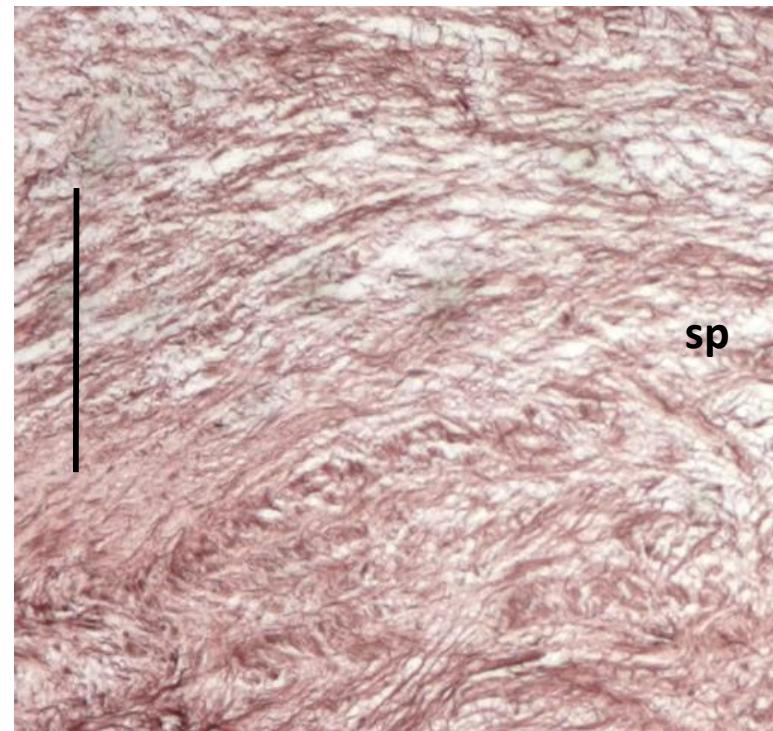


MMV

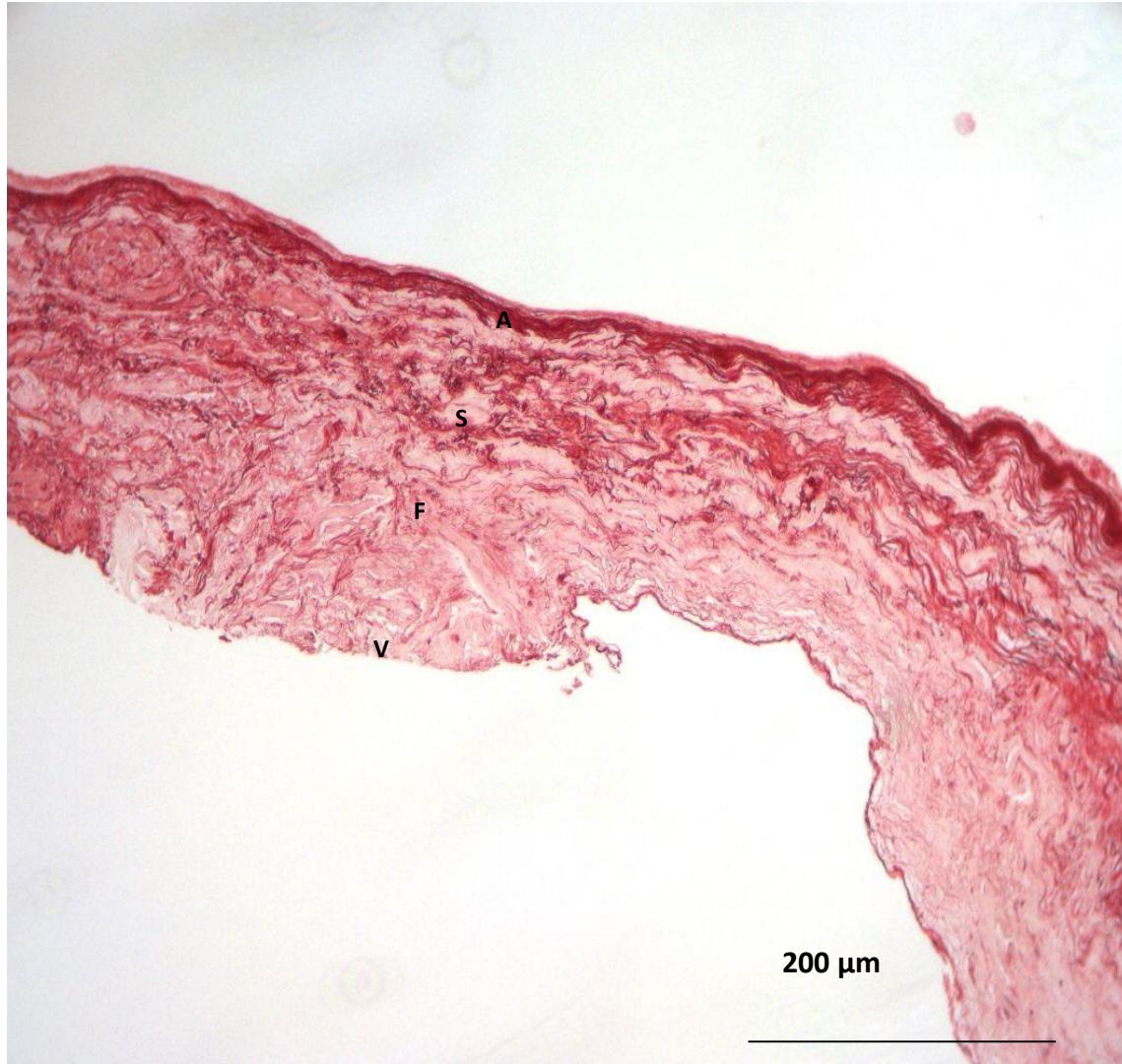
normal



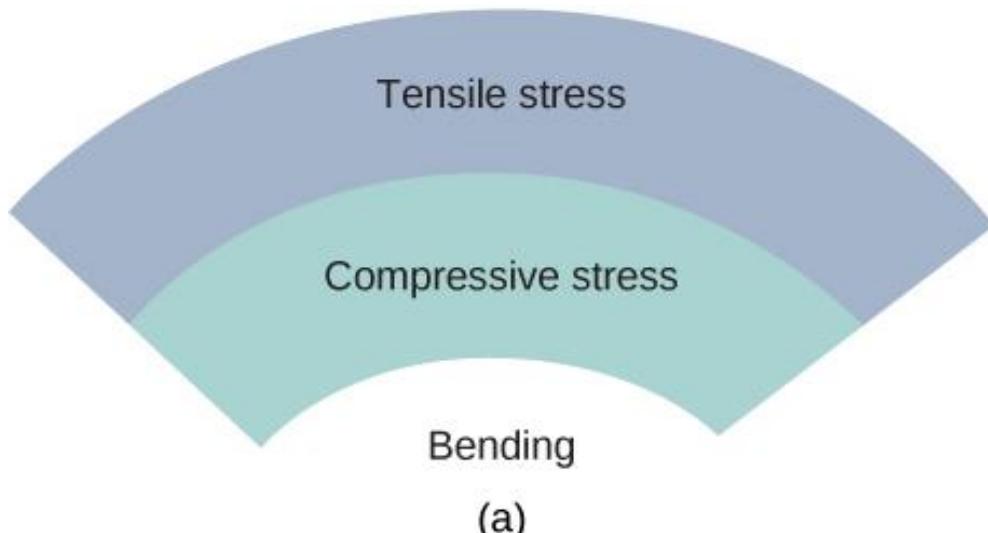
myxomatous



250 μm



Bio-mécanique de la valve mitrale: Stress (tensile and compressive) / strain & shear stress

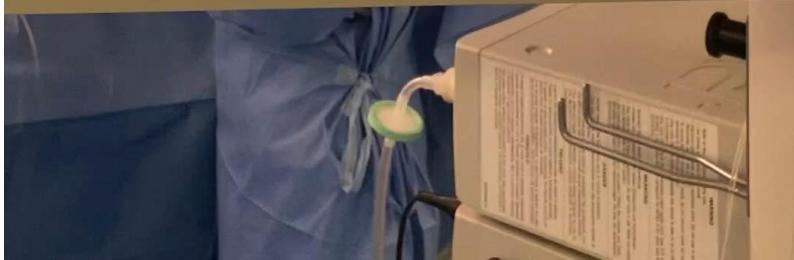
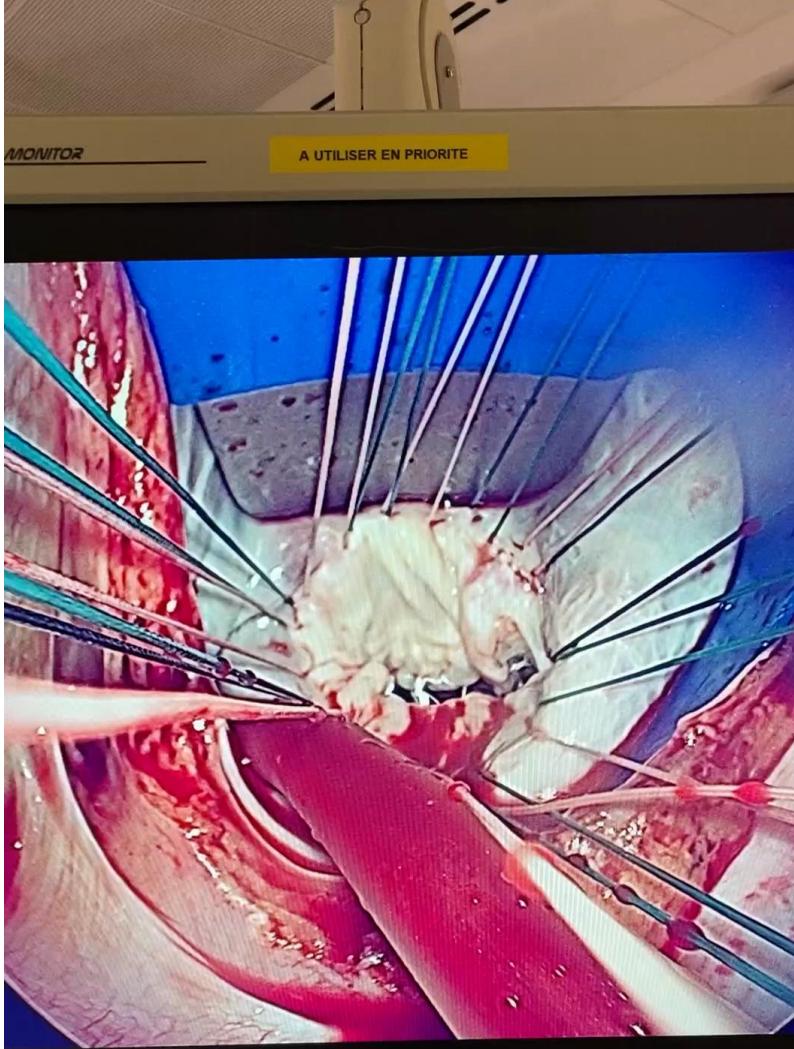


Contre-indications à la chirurgie mitrale vidéo-assistée

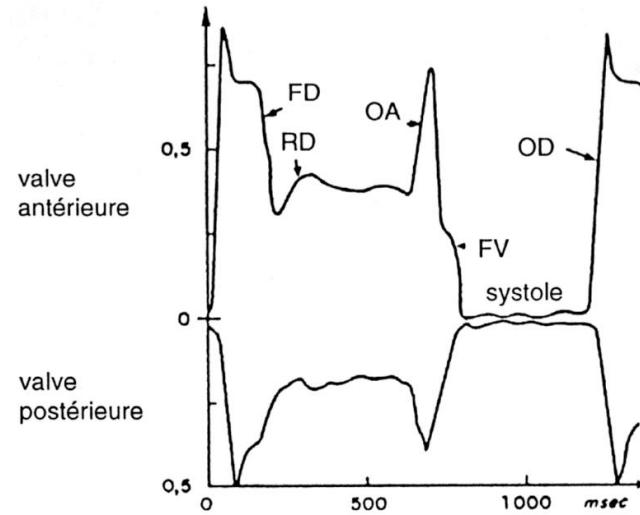
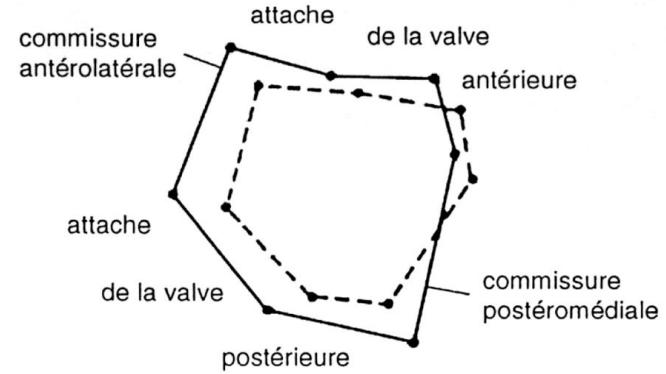
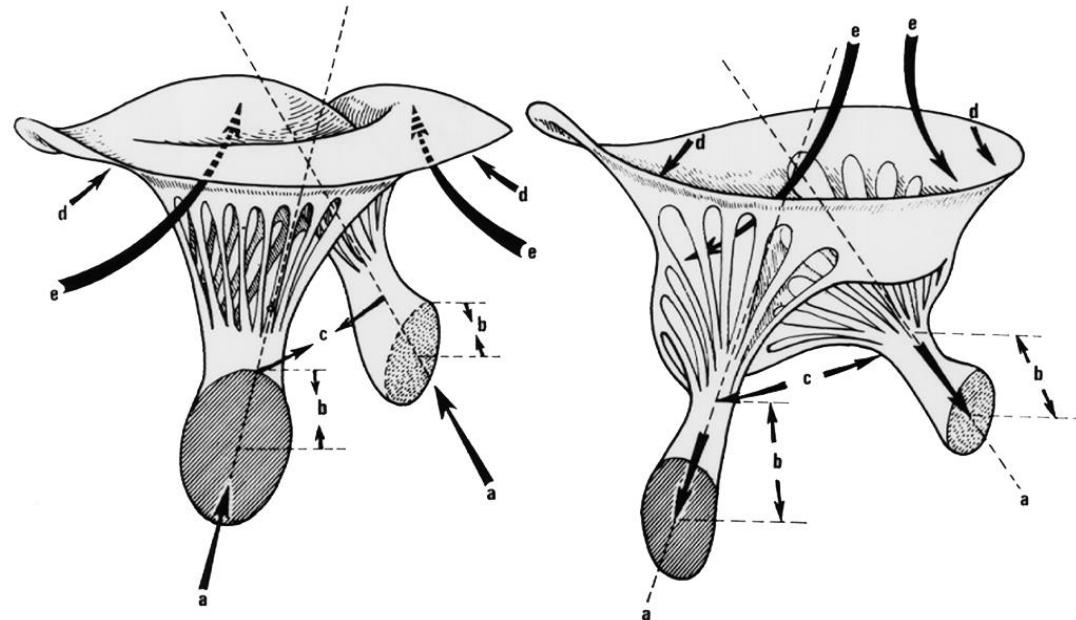
Ca++ anneau mitral et/ou geste associé (RVAo et CABG)

- Previous right thoracotomy
- Significant aortic root/ascending aortic dilatation
- Moderate or severe aortic valve regurgitation
- Fixed pulmonary hypertension (>60 mm Hg)
- Right ventricular dysfunction
- Severe generalized peripheral arterial disease
- Calcification of the aortic root/ascending aorta
- Mitral annular calcification
- Coronary artery disease requiring CABG
- Severe pulmonary dysfunction
- Symptomatic cerebrovascular disease or recent stroke
- Severe liver dysfunction
- Significant bleeding disorder

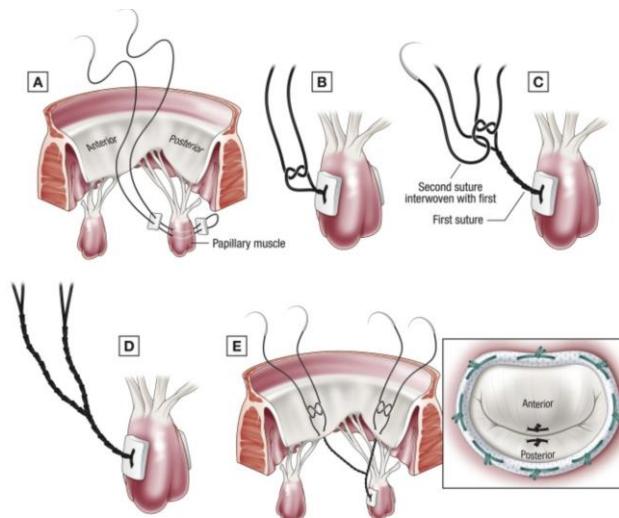


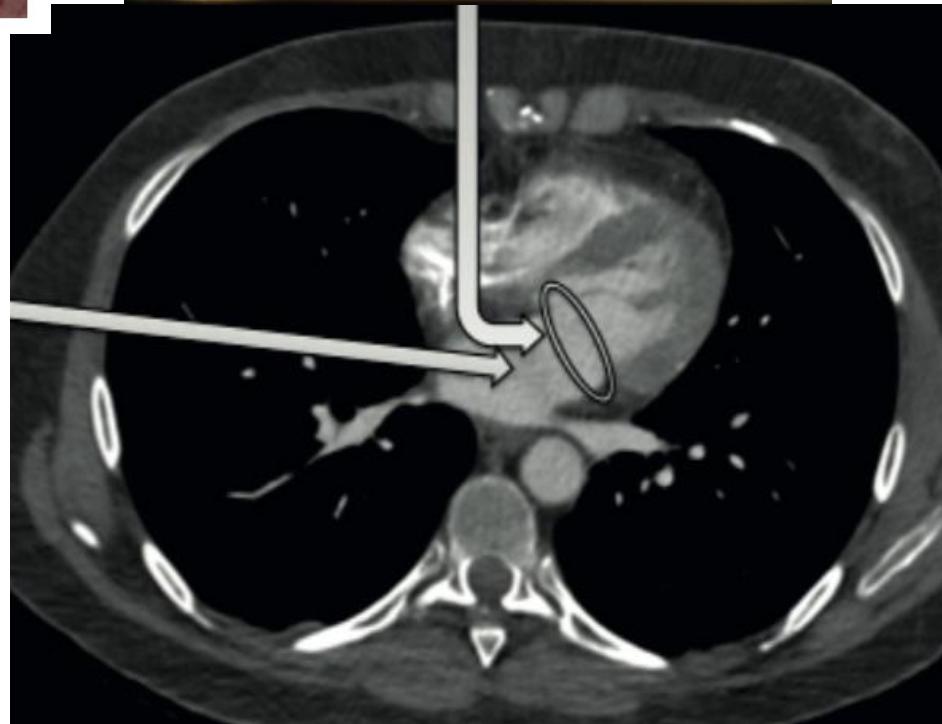
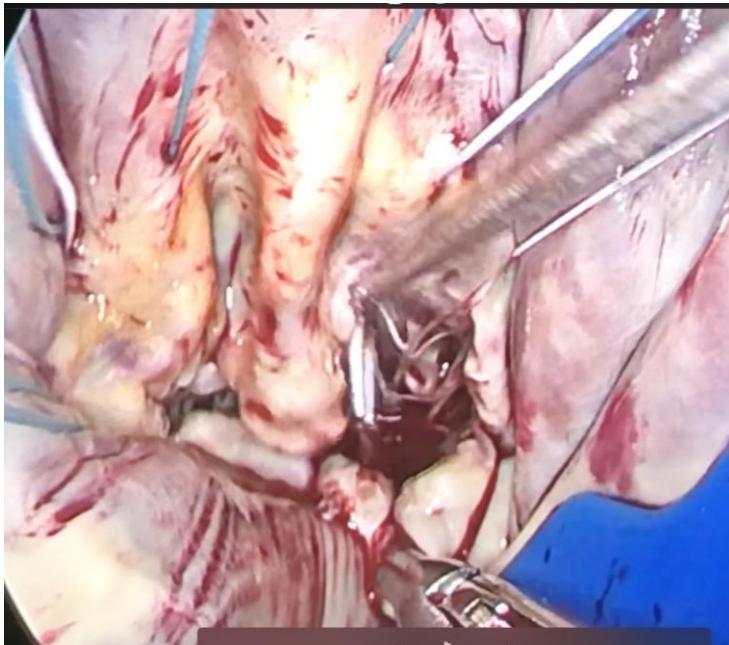
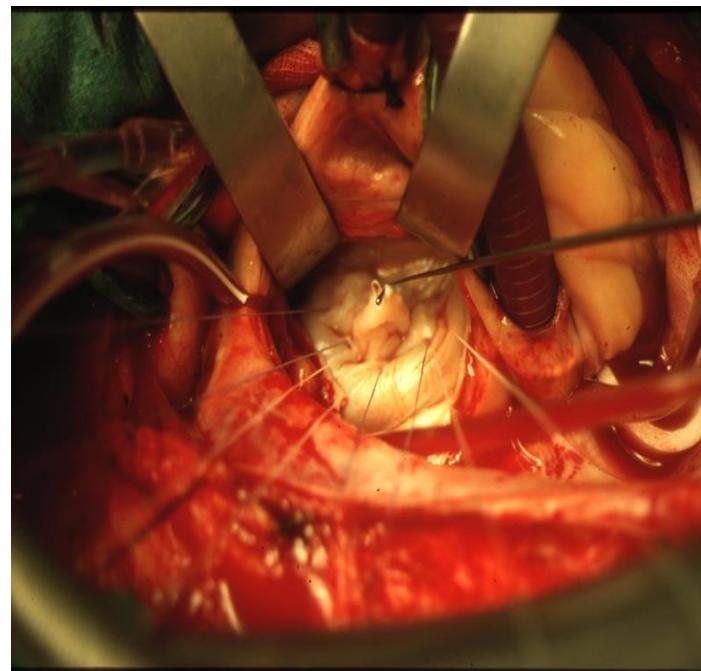
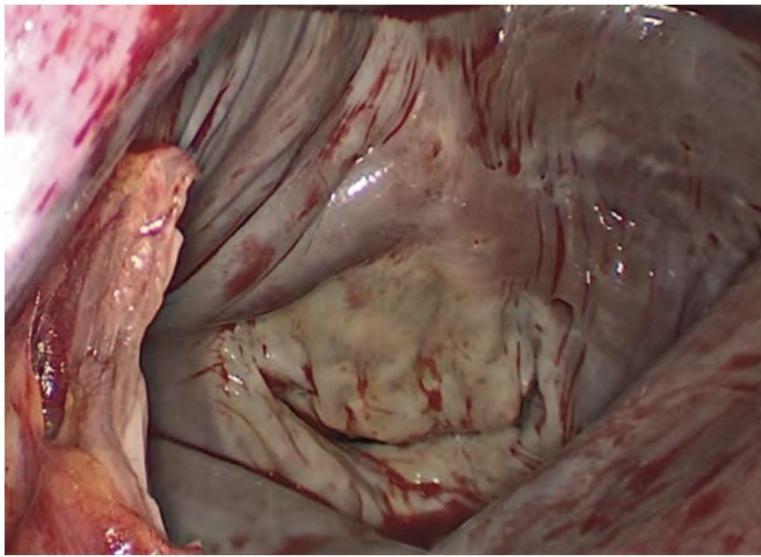


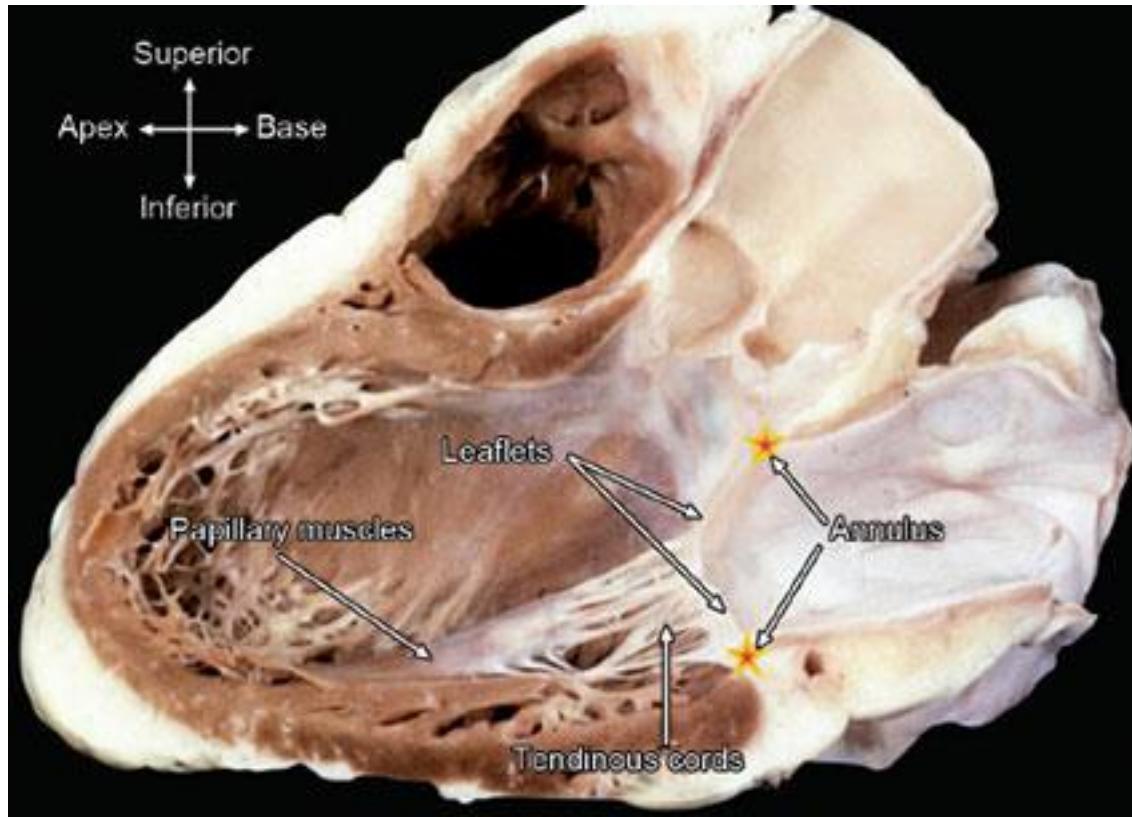
Physiologie de la valvule mitrale



Chirurgie valvulaire mitrale par thoracotomie: *Quel type?*









Type I



Type II



Type IIIa



Type IIIb

Pathologie de la valve mitrale



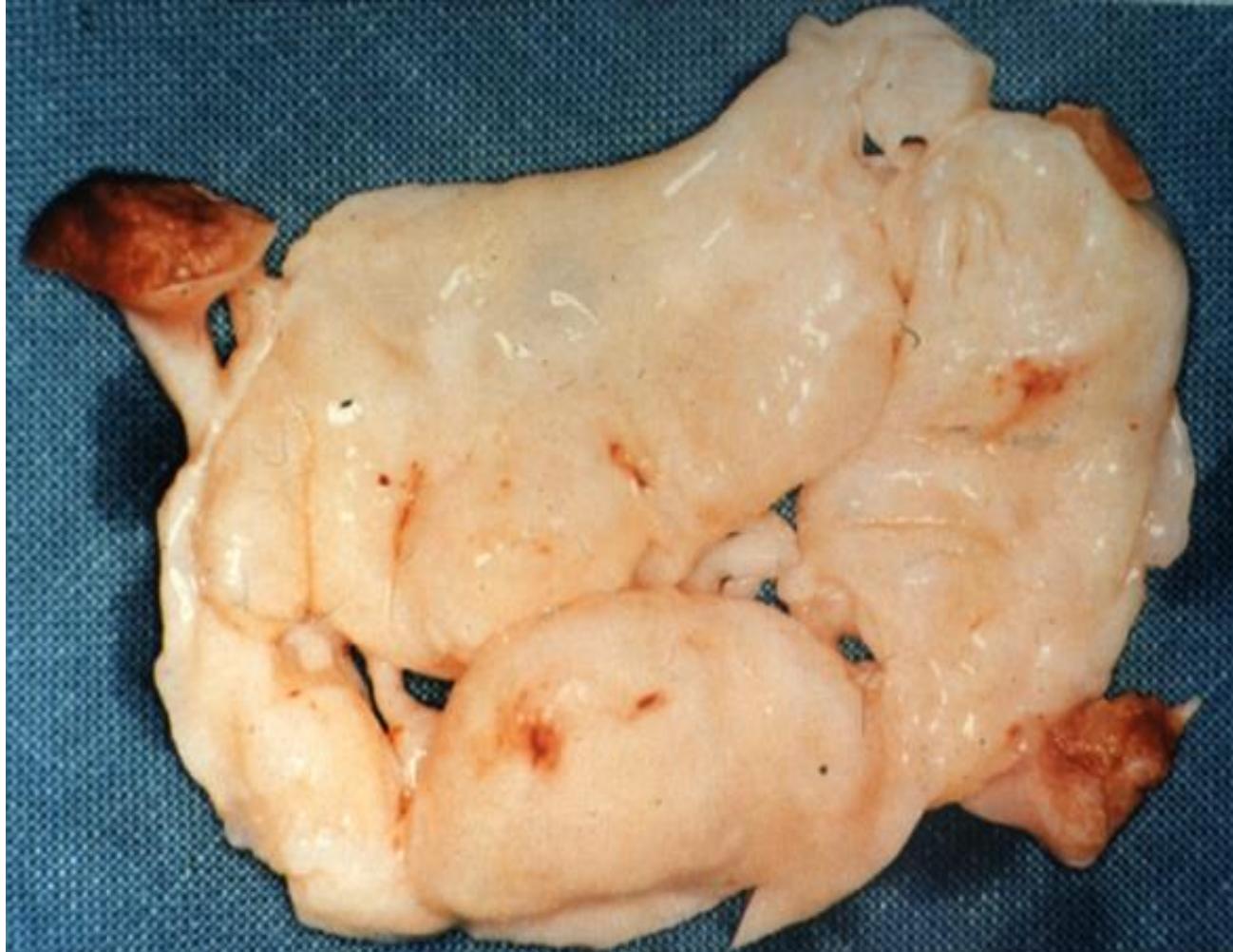
valve rhumatismale

Pathologie de la valve mitrale



dégénérescence fibro-élastique

Pathologie de la valve mitrale

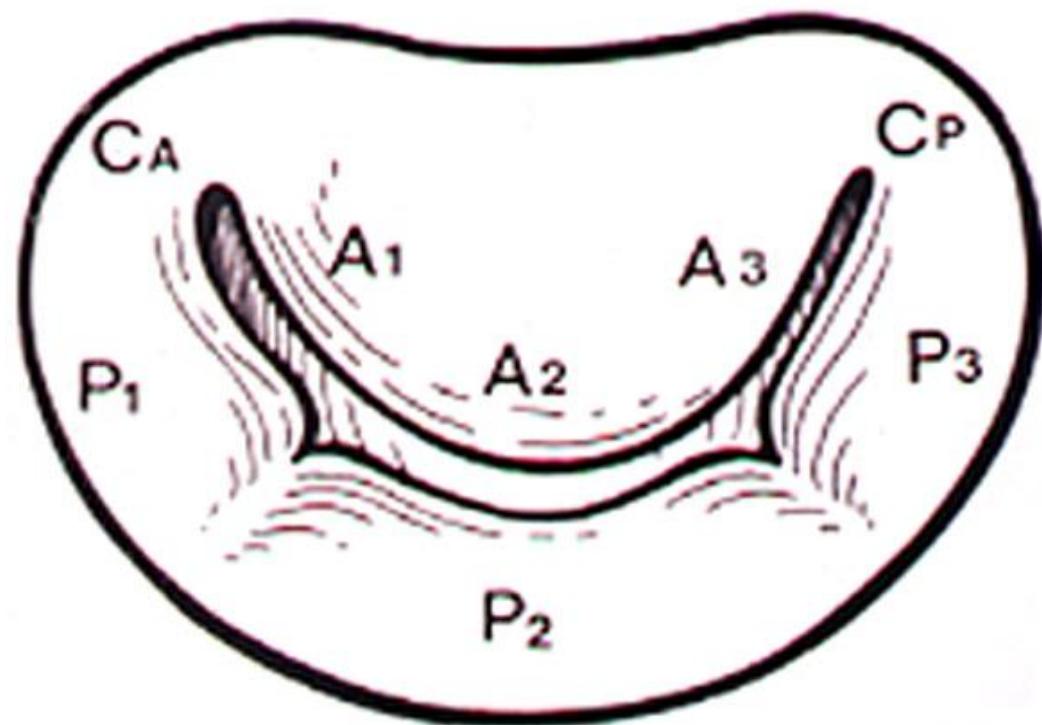
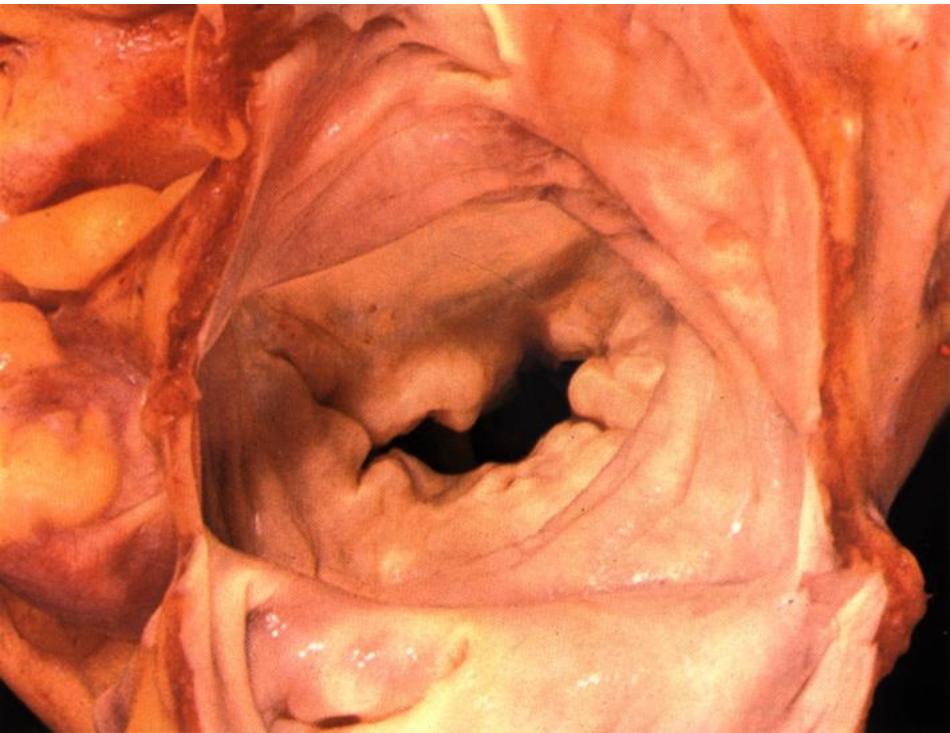


maladie de Barlow

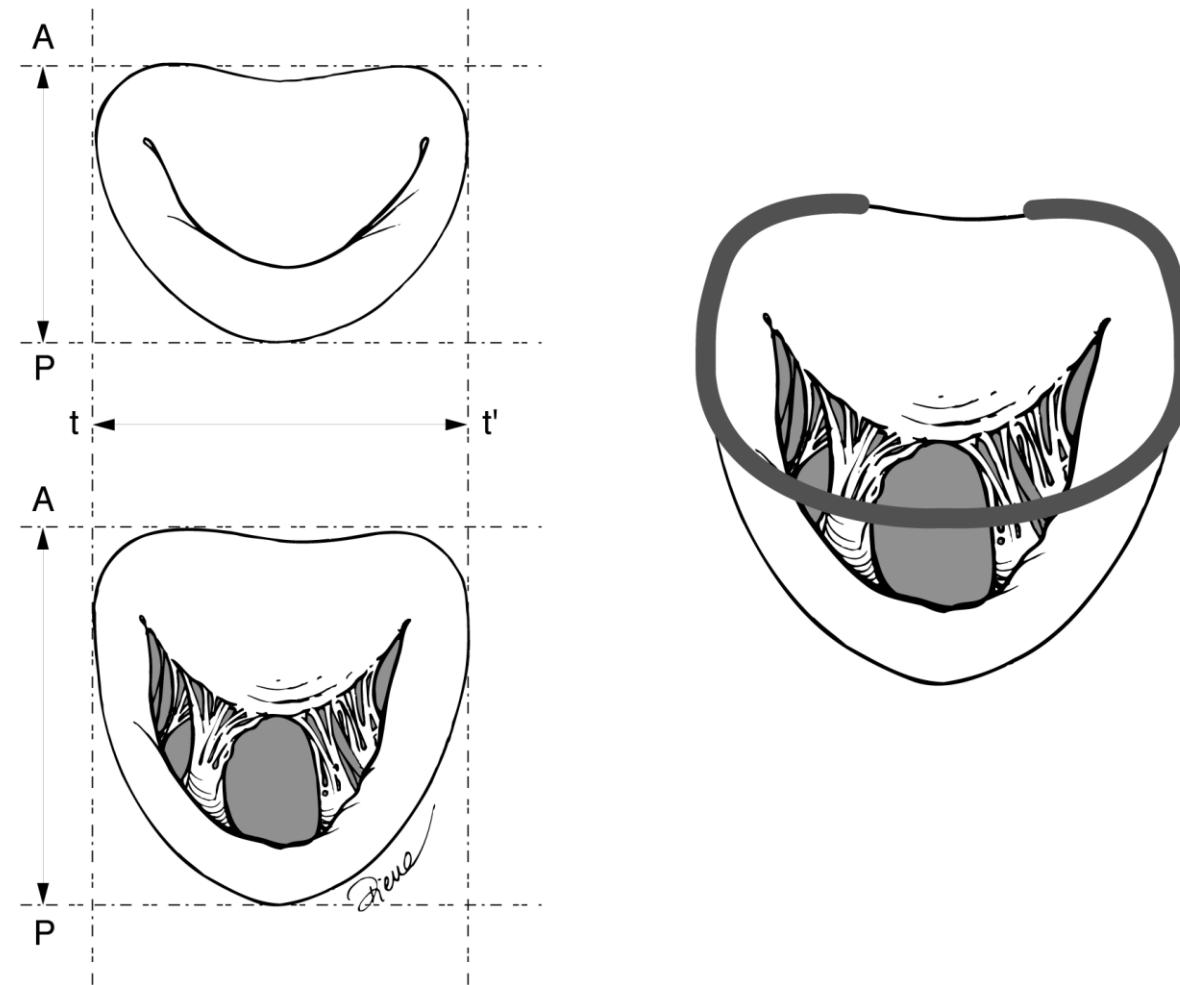
Anatomie de la valvule mitrale



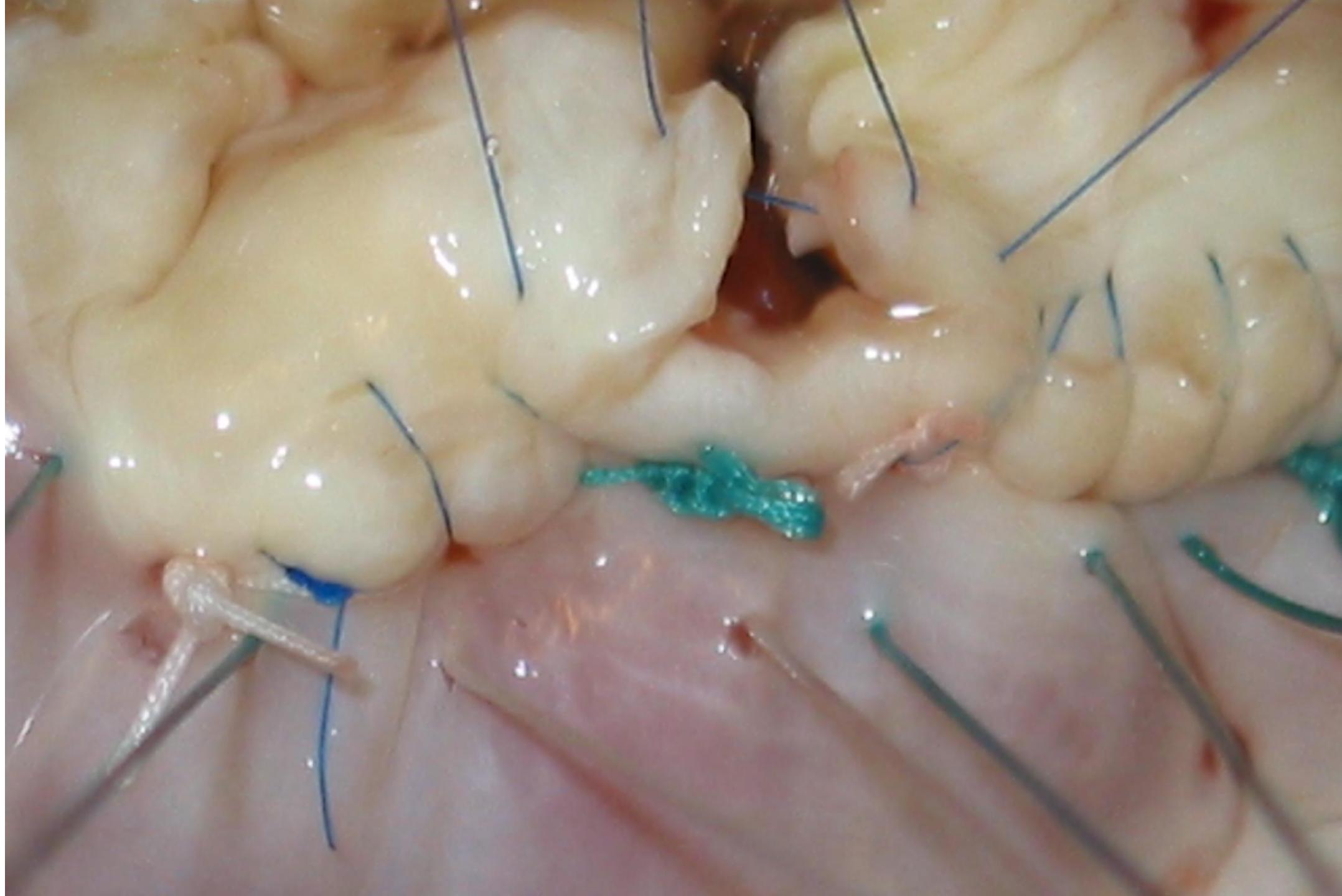


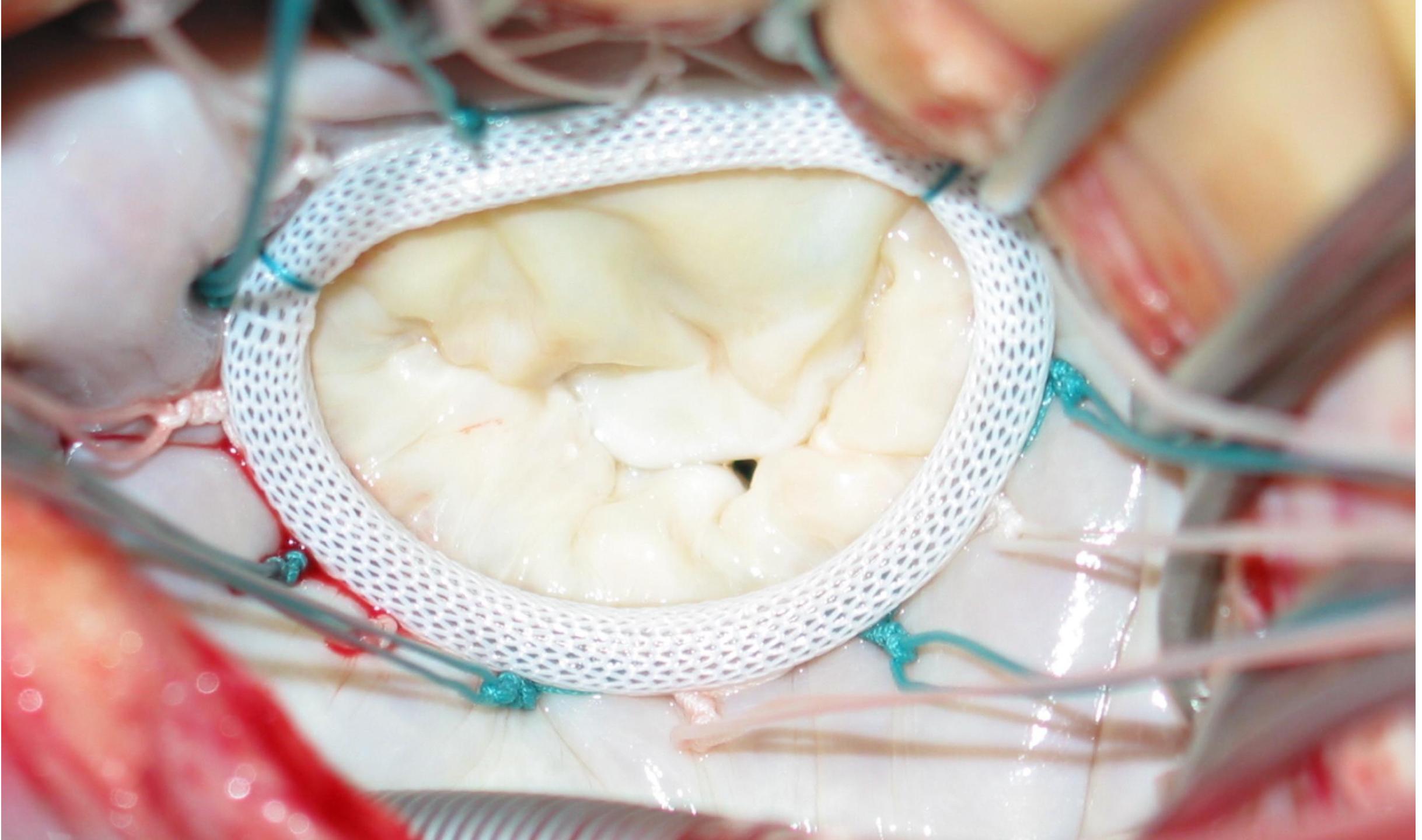


Technique de Réparation Valvulaire

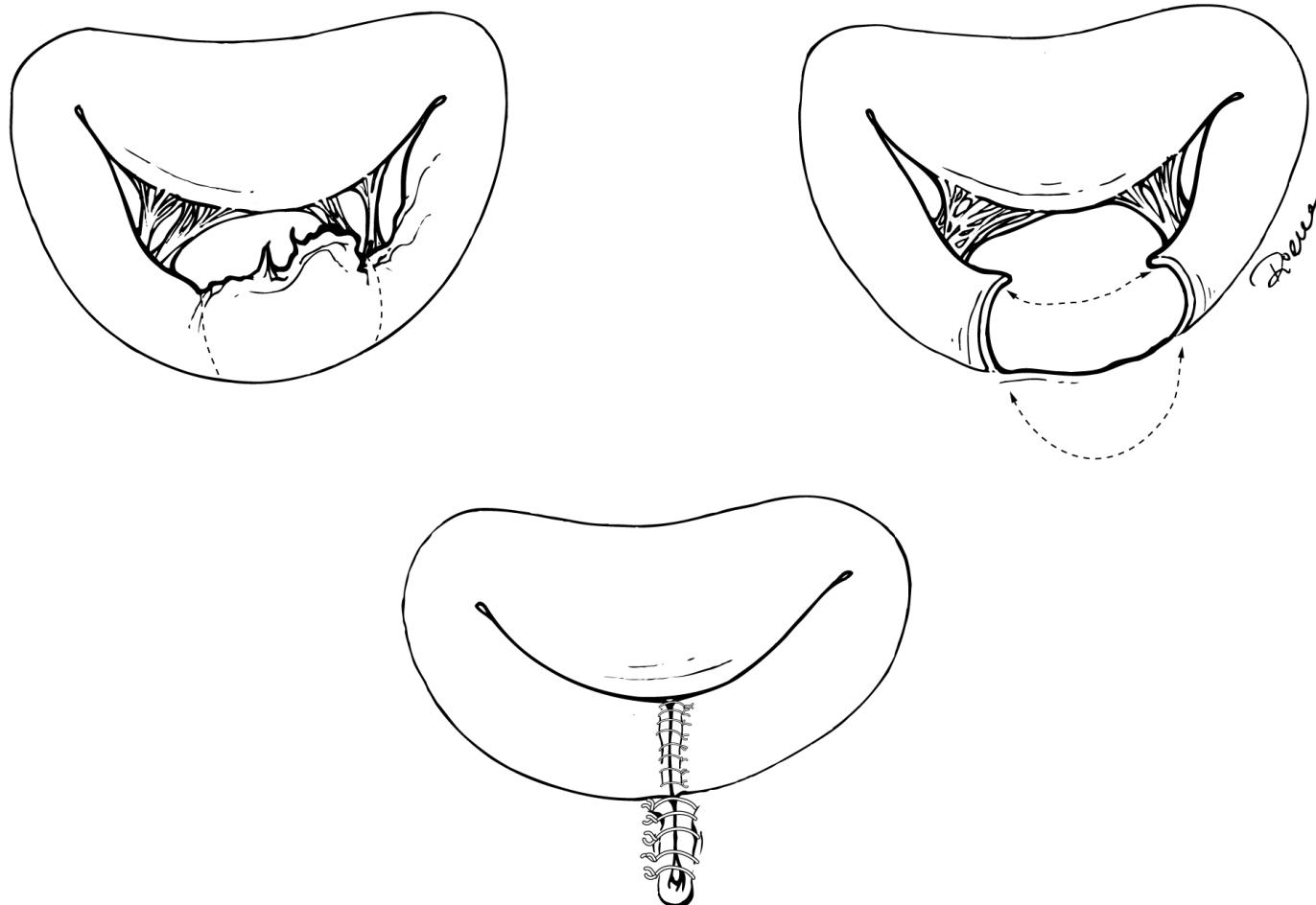


annuloplastie de remodelage



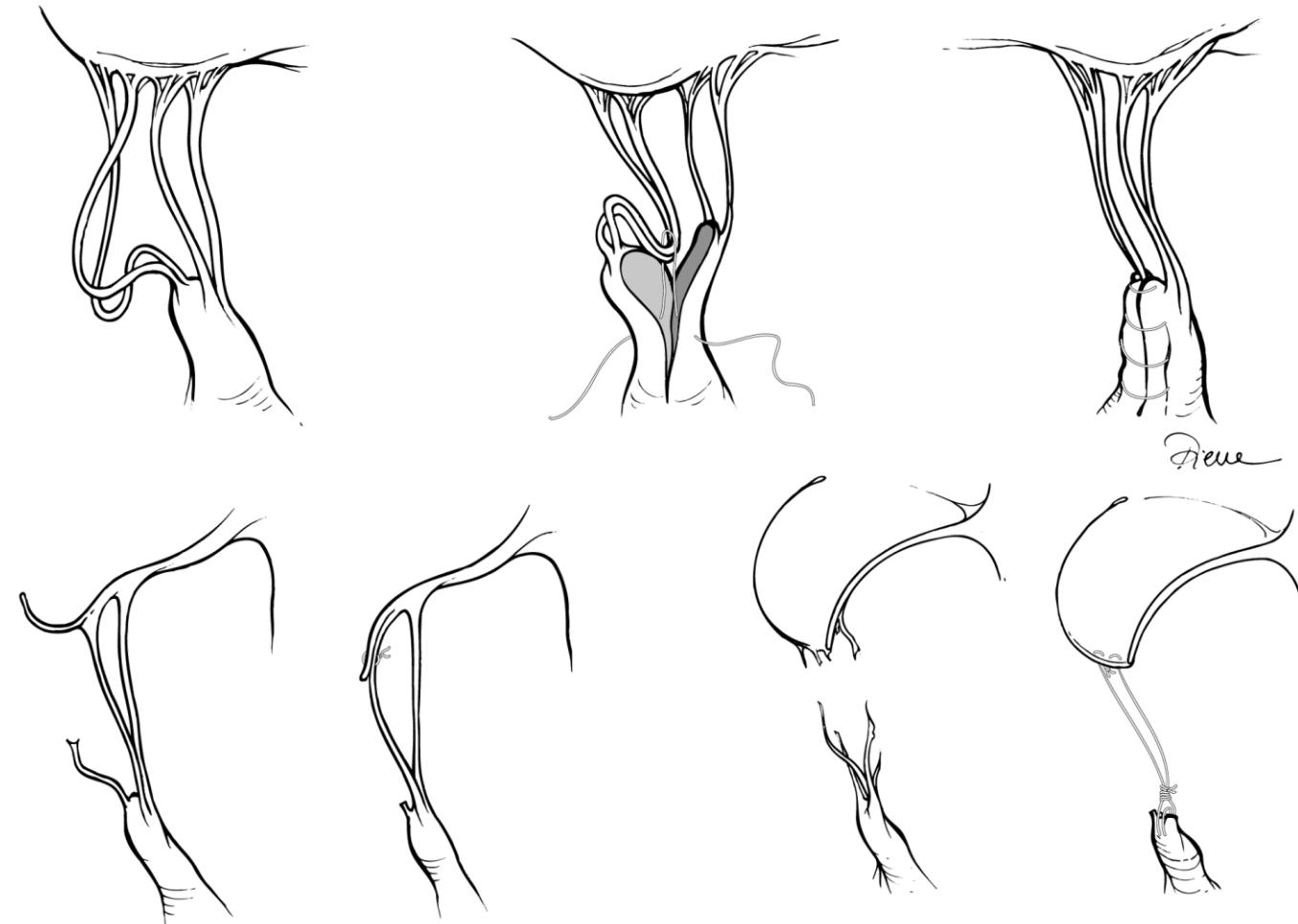


Pathologie de la valve mitrale



résection quadrangulaire

Pathologie de la valve mitrale



chirurgie du prolapsus antérieur

