



Apport du stent à libération du principe actif dans les pathologies vasculaires périphériques

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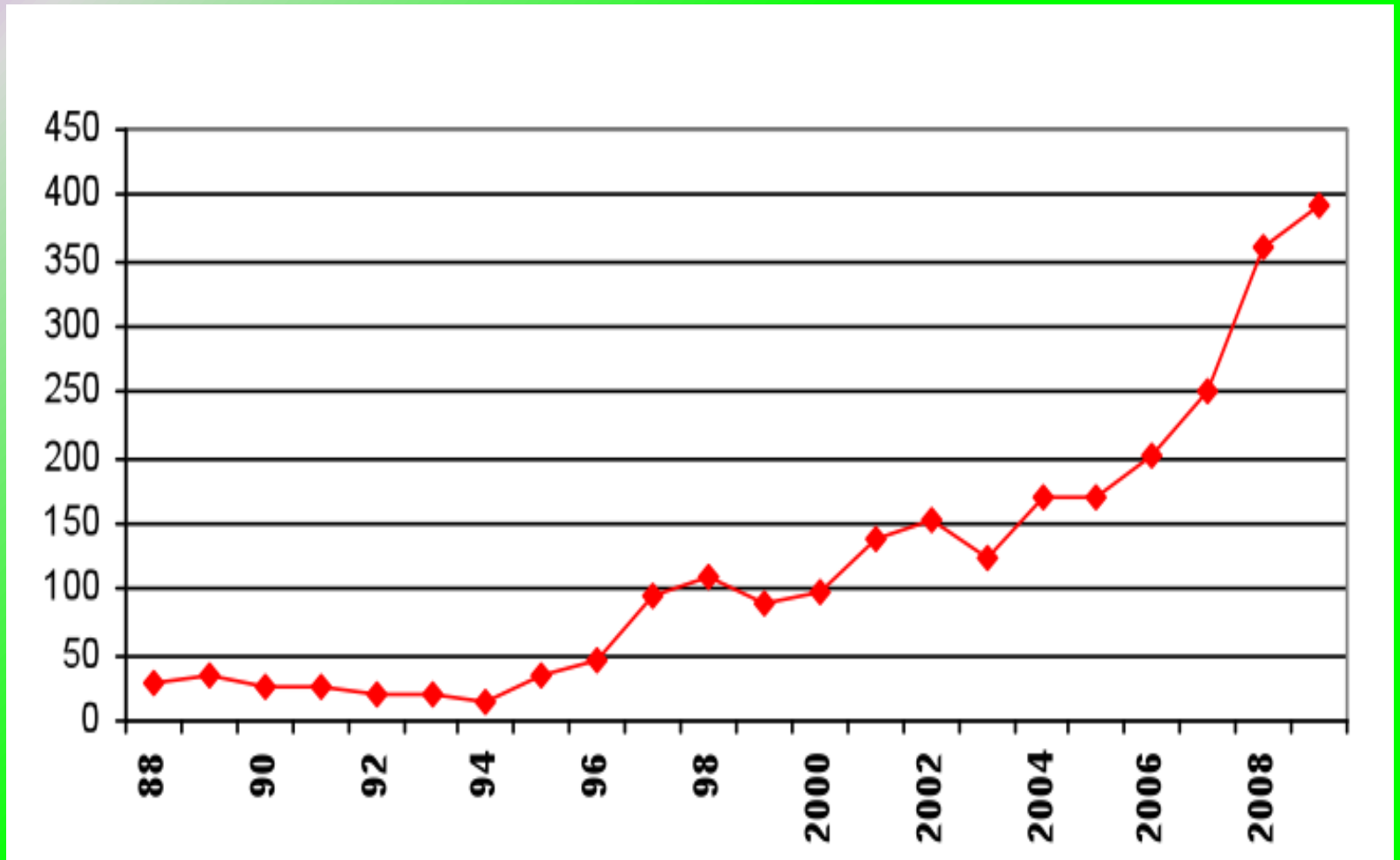
Service de chirurgie vasculaire, CHU de Nantes





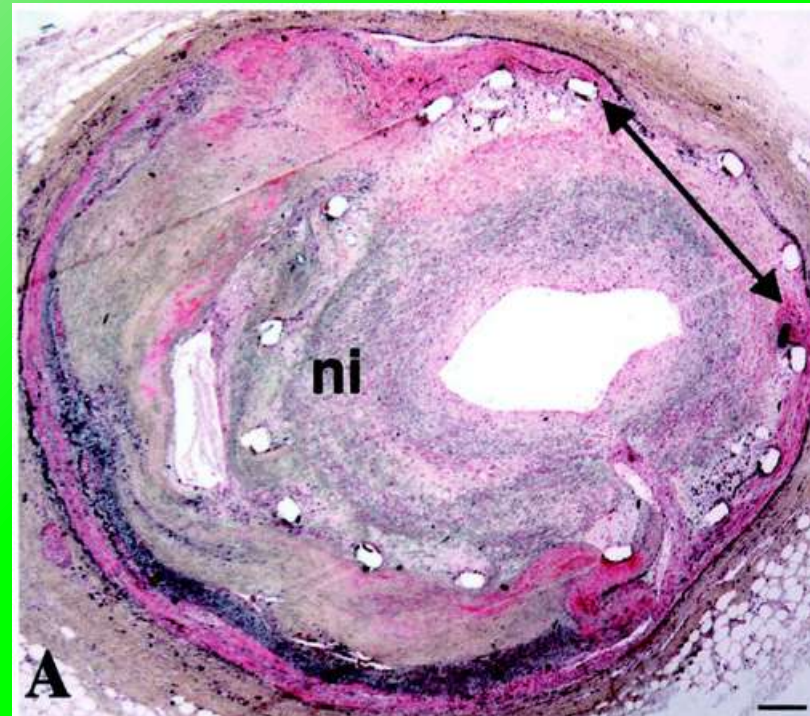
Traitement endovasculaire périphérique

Angioplasties



Un talon d'Achille: la resténose intra-stent

Inflammation / CML / MEC



Hoffmann. *Circulation*, 1996



Phénomène local

Echec des traitements systémiques

Stent à libération de principe actif



Etude RAVEL: 0% de resténose à 9 mois !

Stockohlm, ESC 2001

The New England Journal of Medicine

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**A RANDOMIZED COMPARISON OF A SIROLIMUS-ELUTING STENT
WITH A STANDARD STENT FOR CORONARY REVASCULARIZATION**



Stents actifs et pathologies vasculaires périphériques

SFA:	20% @ 18 mo	Duda, J Endovasc Ther, 2005
Vertébrale:	62.5% @ 6 mo	Lugmayr, Rofo, 2004
Rénale:	18.7% @ 6 mo	Rabbia, CIRSE conference, 2006
Infra-poplitées:	37% @ 12 mo	Siablis, J Endovasc Ther, 2005



– **STRIDES study** (everolimus) –
Abbott

– **Zilver PTX study** (paclitaxel) –
COOK



STRIDES (abbott)

SFA Treatment with Drug-Eluting Stents study

- Design:** Registre prospectif (104 patients inclus; 11 sites participants)
- Stent:** Dynalink
- Drogue:** Everolimus (225 $\mu\text{g}/\text{cm}^2$)
- Polymère:** EVAL polymère
- Inclusion:** lésions de novo de l'AFS et de l'artère poplitée haute; Rutherford 2-5
- Suivi:** 1 an





ZILVER PTX (cook)

Design: Etude randomisée ATL / Zilver PTX (479 patients); 55 sites

Stent: Zilver Flex

Drogue: Paclitaxel (300 $\mu\text{g}/\text{cm}^2$)

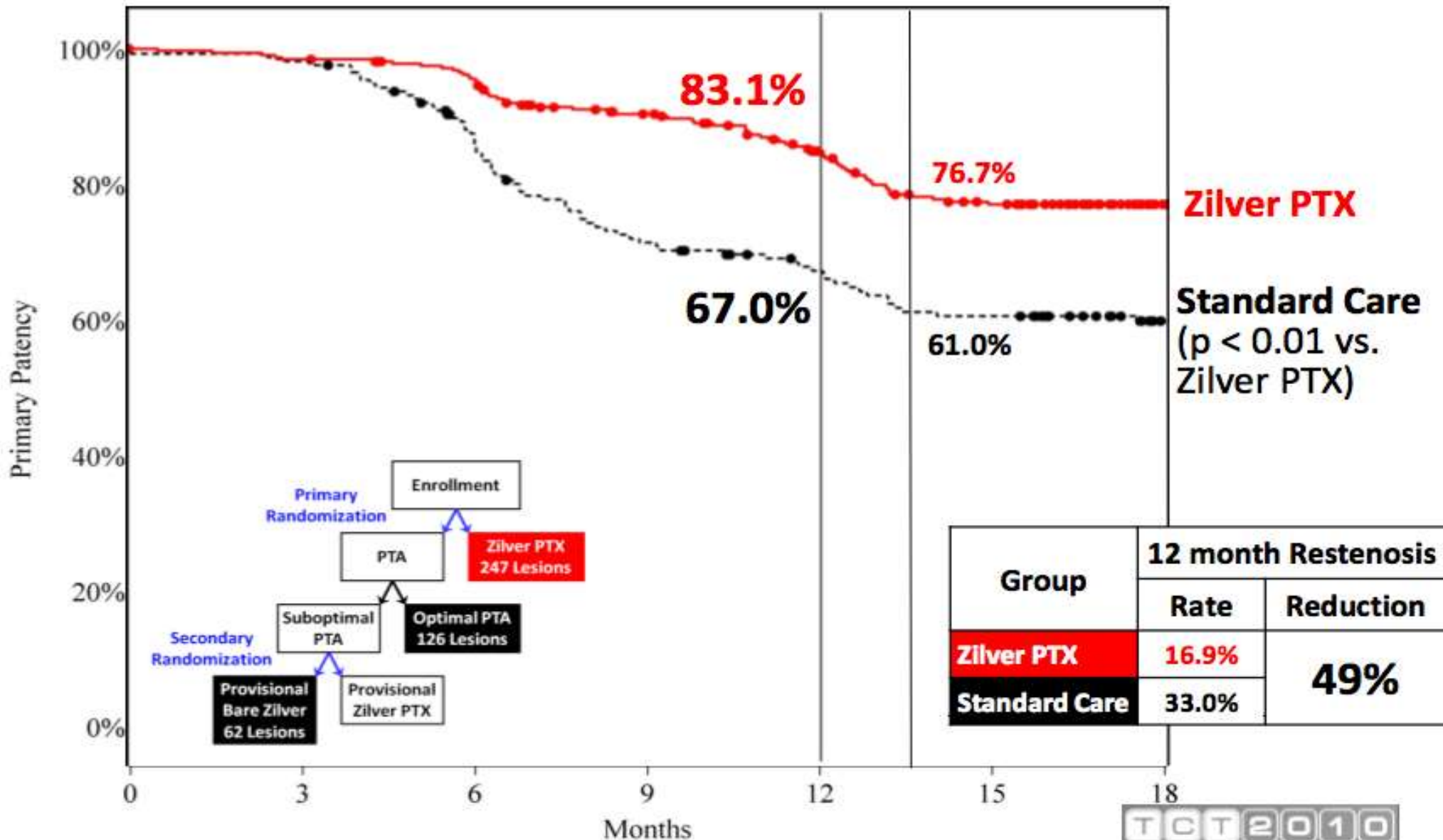
Polymère: /

Inclusion: Lésions de novo de l'AFS et de l'artère poplitée haute; Rutherford 2-6

Critère : Perméabilité à 12 mois

Suivi: 5 ans

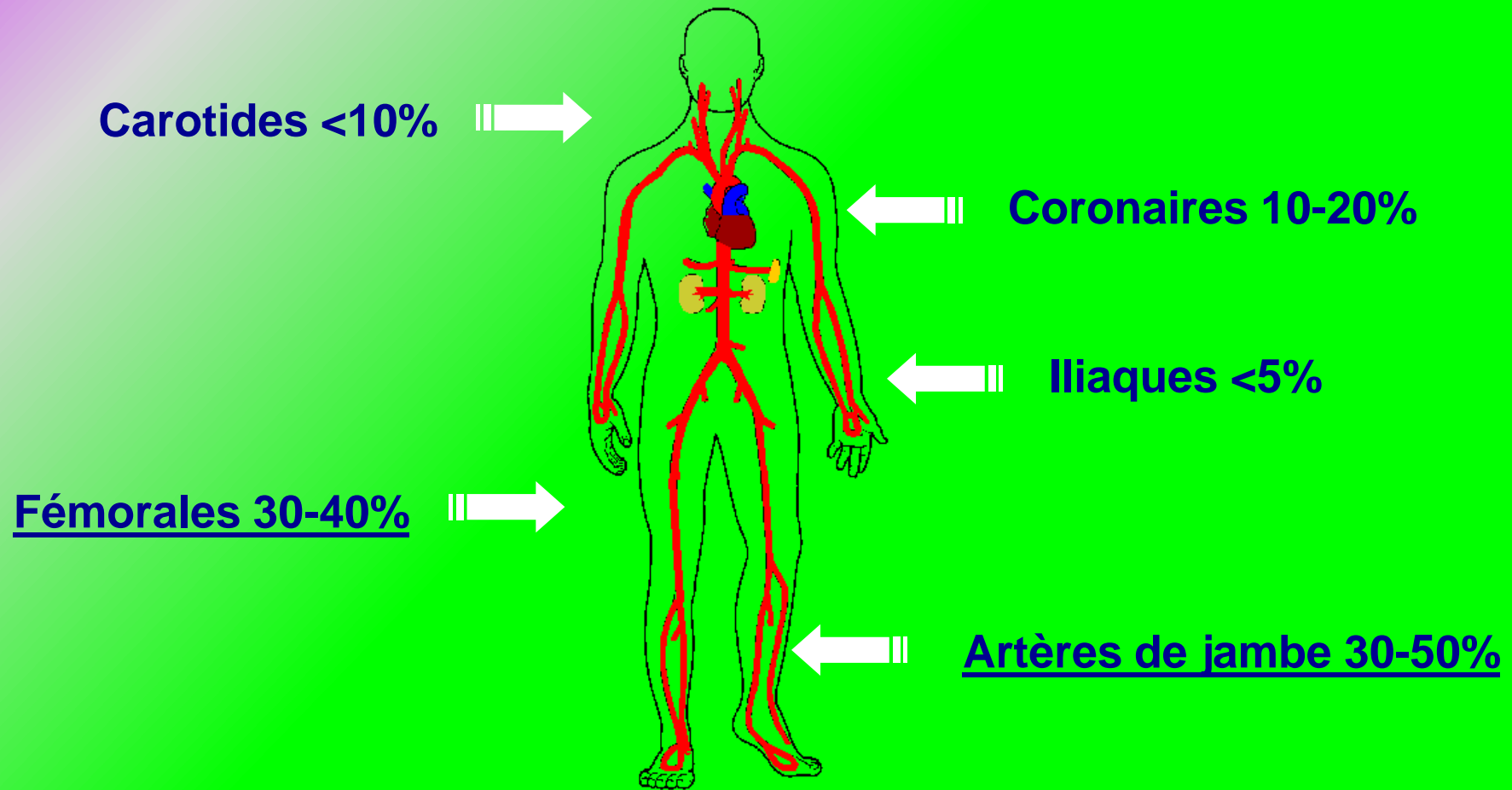
Patency (PSVR < 2.0) for Primary Zilver PTX vs. Standard Care (PTA with Provisional Bare Stenting)





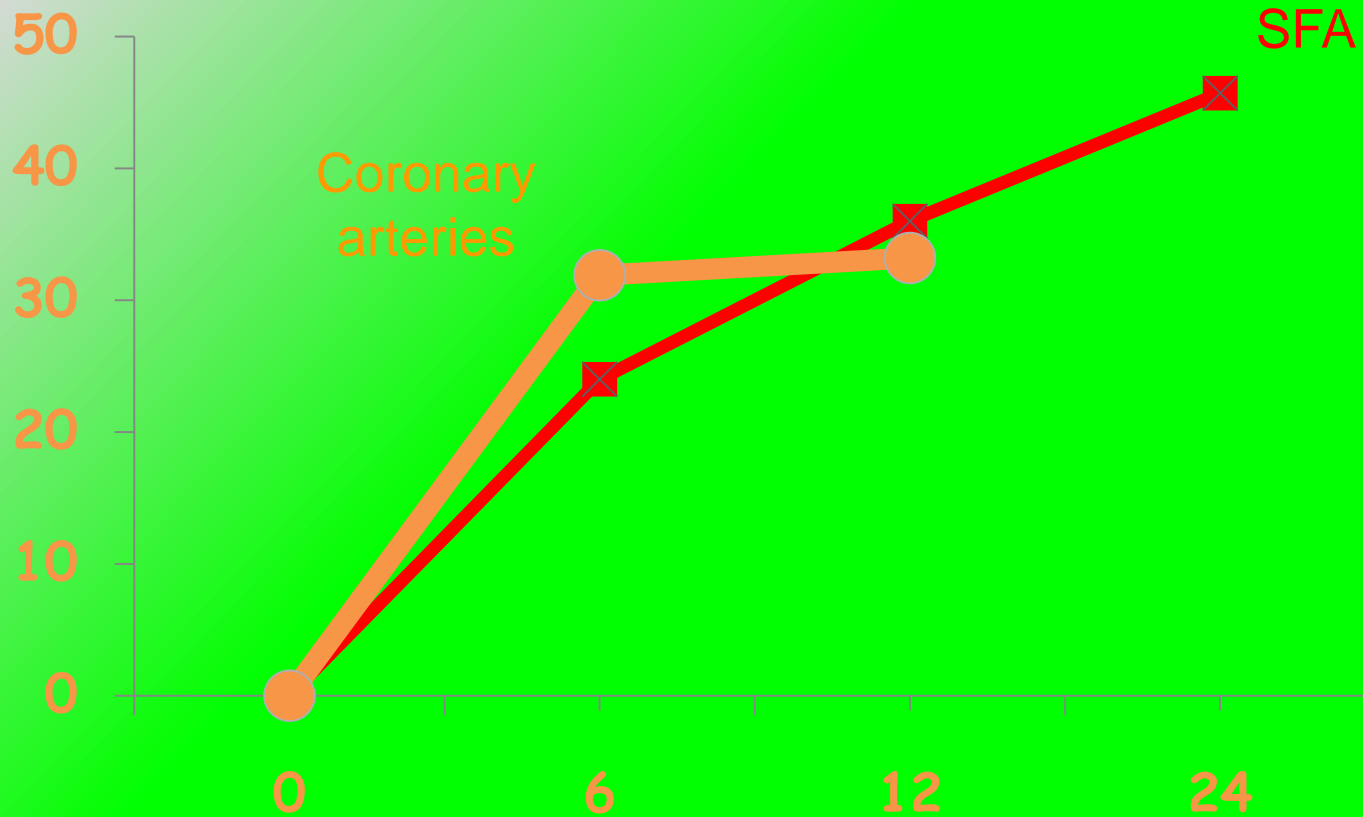
Hétérogénéité du réseau artériel

La survenue de la resténose intra-stent varie selon les territoires artériels



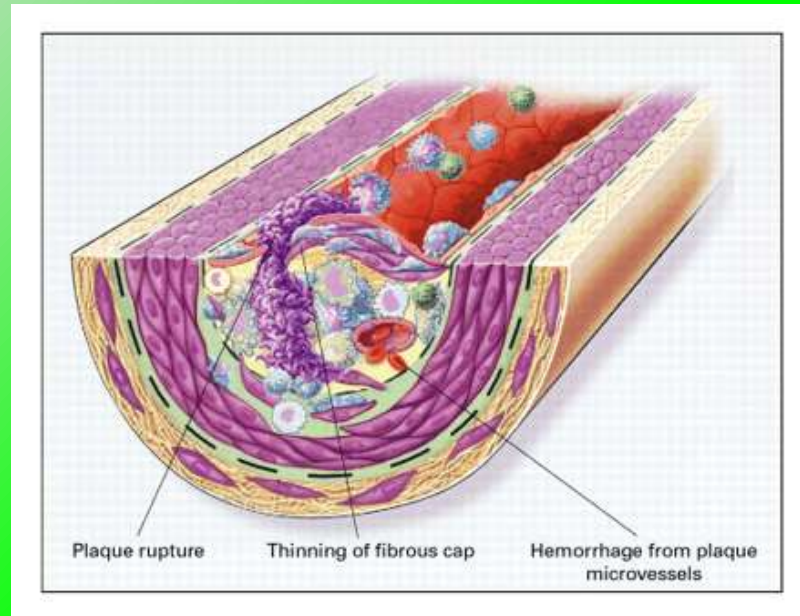


Cinétique de la resténose



Kastrati A, *Circulation*, 1993; Schillinger, *Circulation*, 2007

La nature de la paroi artérielle influence la diffusion de la drogue



Artères élastiques >>> artères musculaires

Thrombus

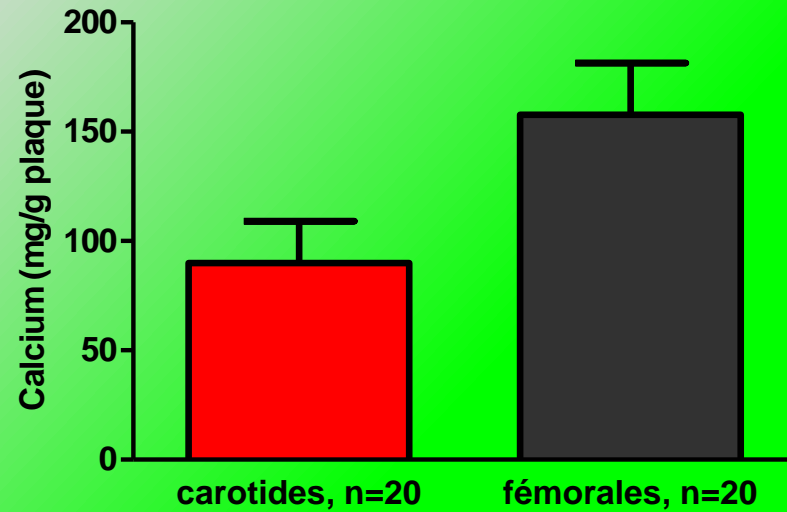
(Hwang, Circ Res, 2002) (Hwang, Circulation, 2005)



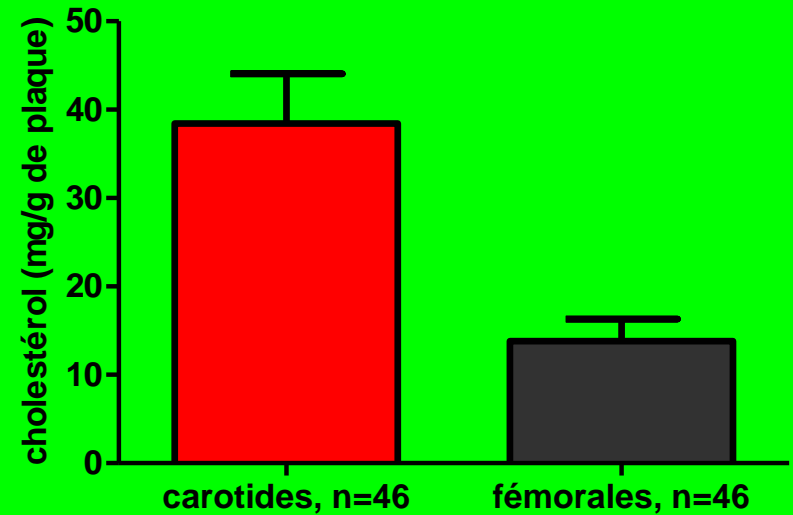
ECLA

(Etude Comparative des Lésions Athéromateuses)

Calcium



Lipides



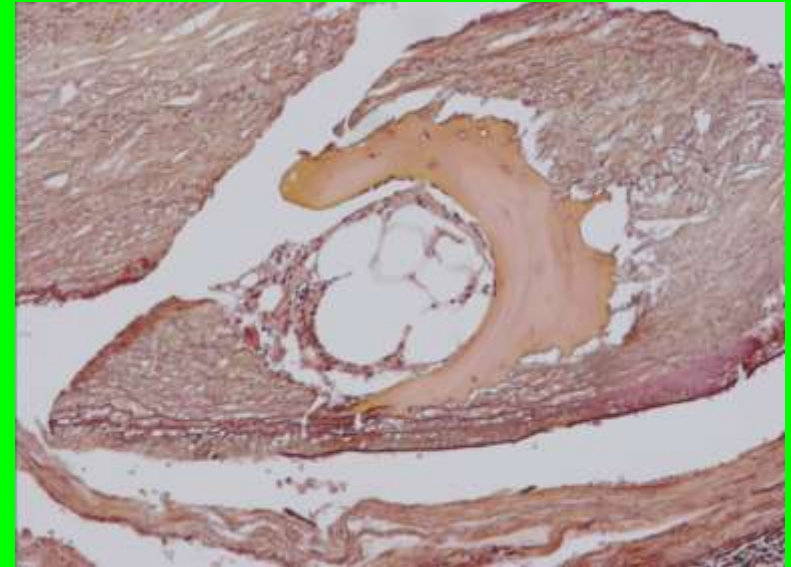
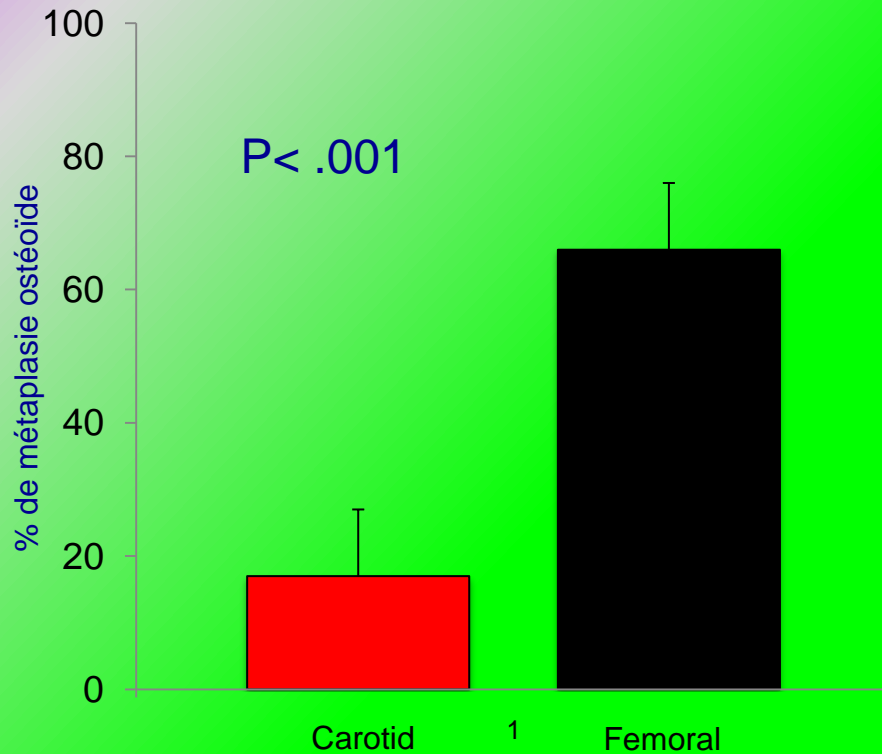
Hérisson et al, submitted



ECLA

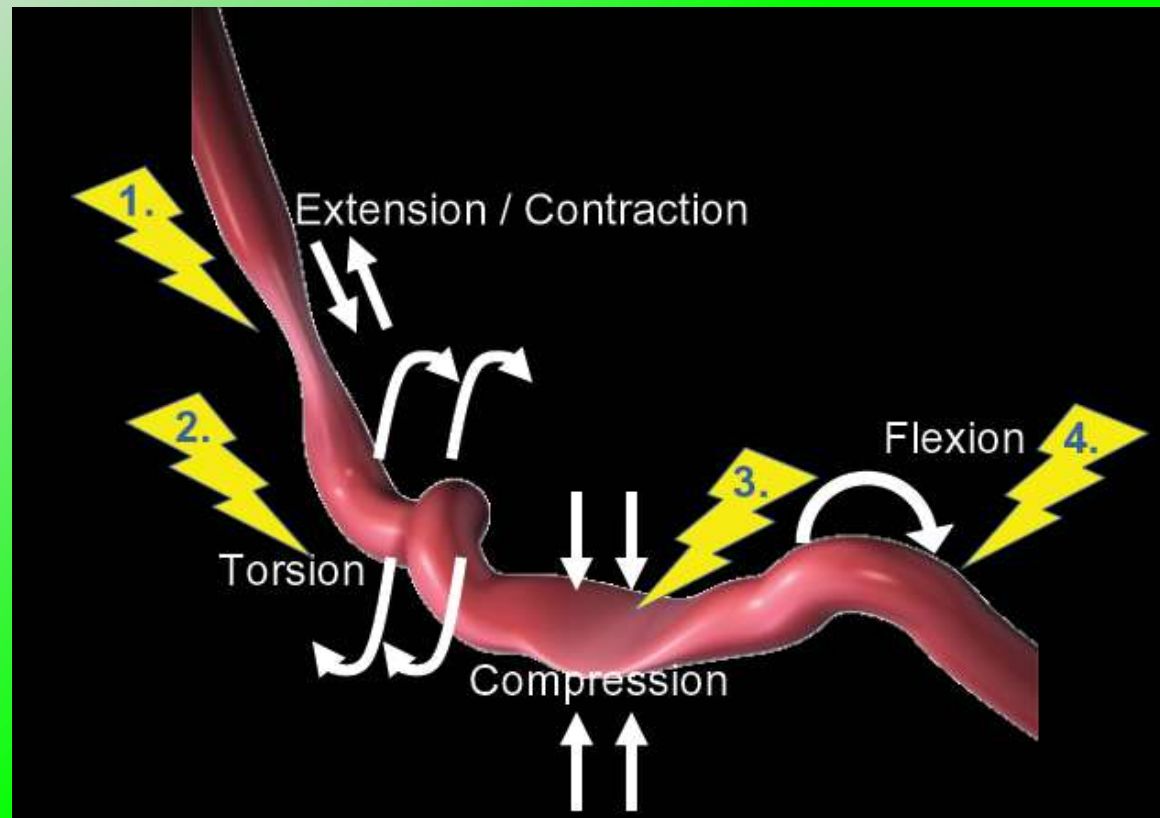
(Etude Comparative des Lésions Athéromateuses)

Métaplasie ostéoïde



Hérisson et al, submitted

Contraintes physiques (fractures – malaposition)



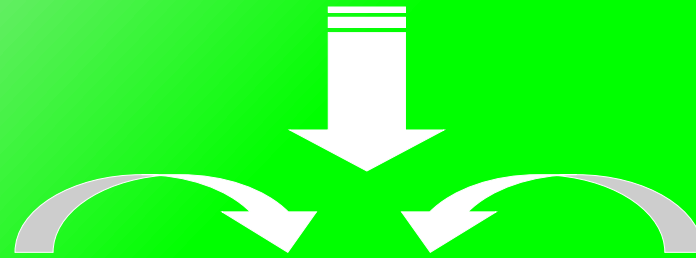
Hara, Adv Drug Deliv Rev, 2006



Stent actif

STENT

DROGUE



POLYMERE

EFFICACITE

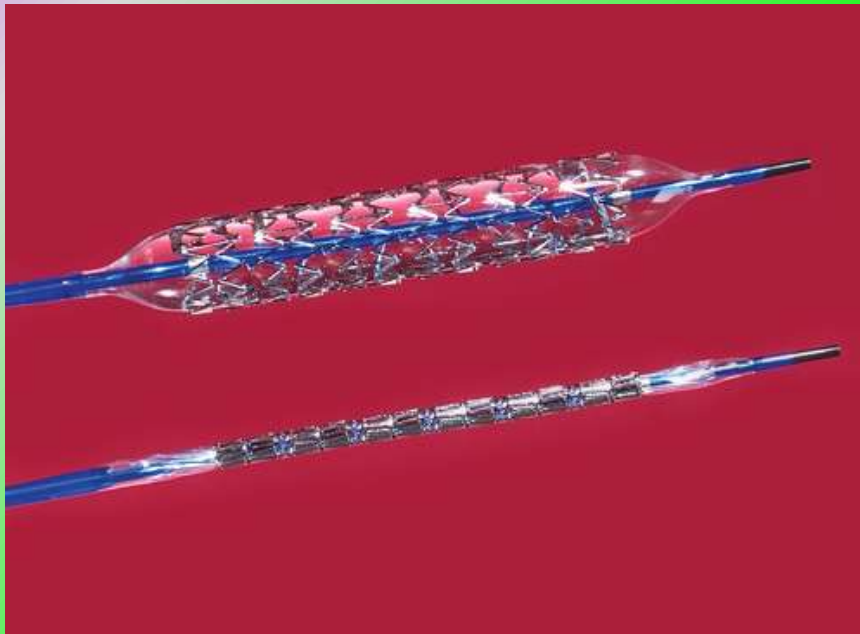
TOLERANCE



Stent

Acier

Nitinol



Rogers, Circulation, 1995



Cellules fermée

Cellules ouvertes

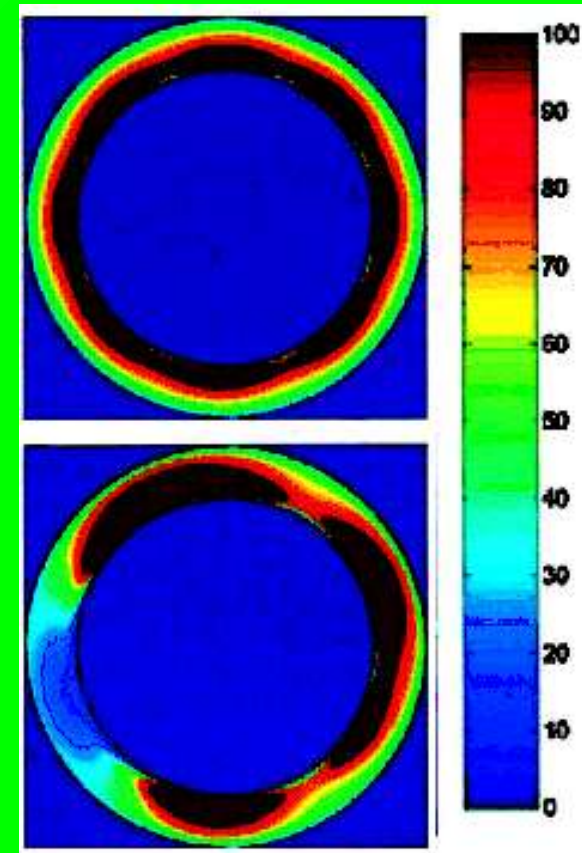


Rev Cardiovasc Med, 2005

Le design du stent détermine la distribution de la drug

Distribution homogène des barreaux

Distribution inhomogène des barreaux



Hwang, *Circulation*, 2001



Sirolimus - Paclitaxel

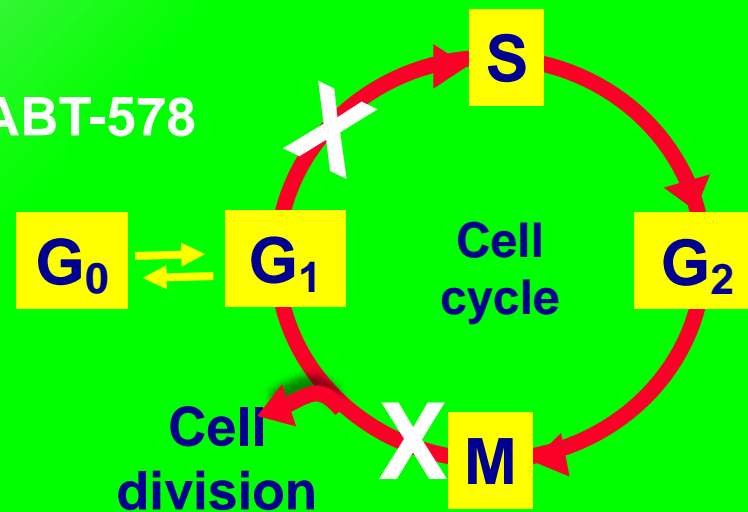


Cytostatique



Cytotoxique

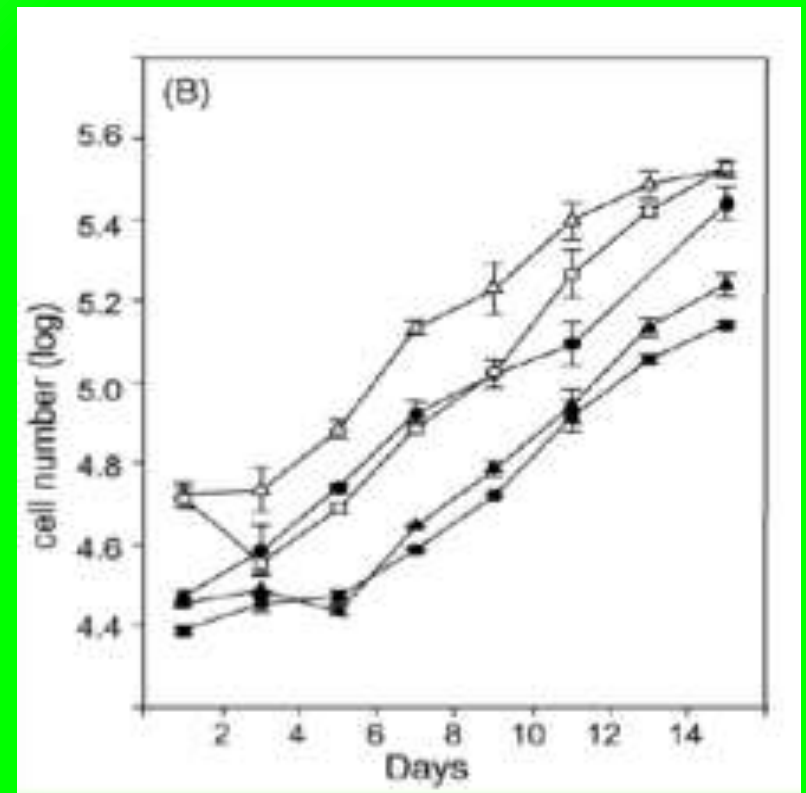
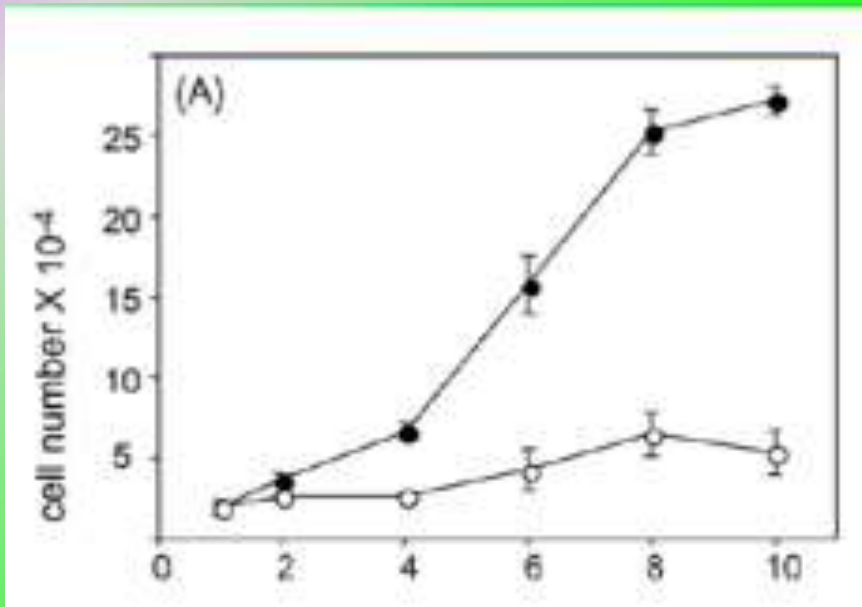
Sirolimus, Everolimus, ABT-578



Paclitaxel



SRL et prolifération cmlv





Conclusions

Peu de preuves de l'intérêt des stents actifs en pathologie vasculaire périphérique

Spécificité des artères périphériques

Critères de jugements

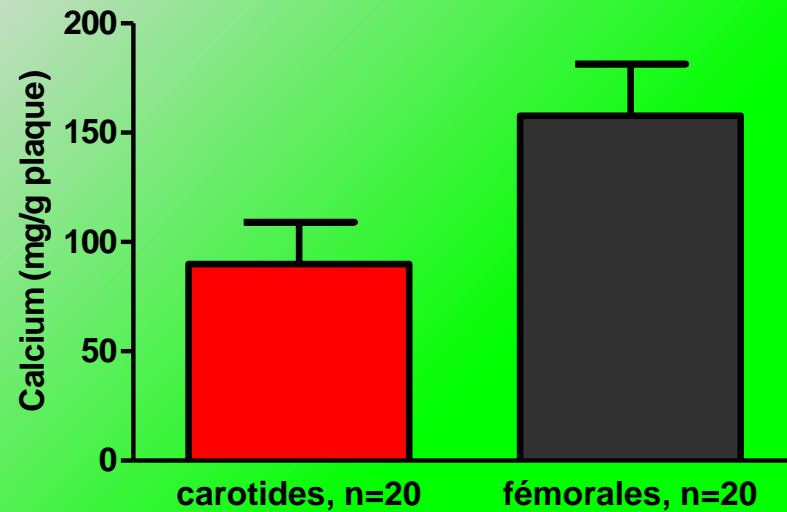
Périmètre de marche / sauvetage de membre



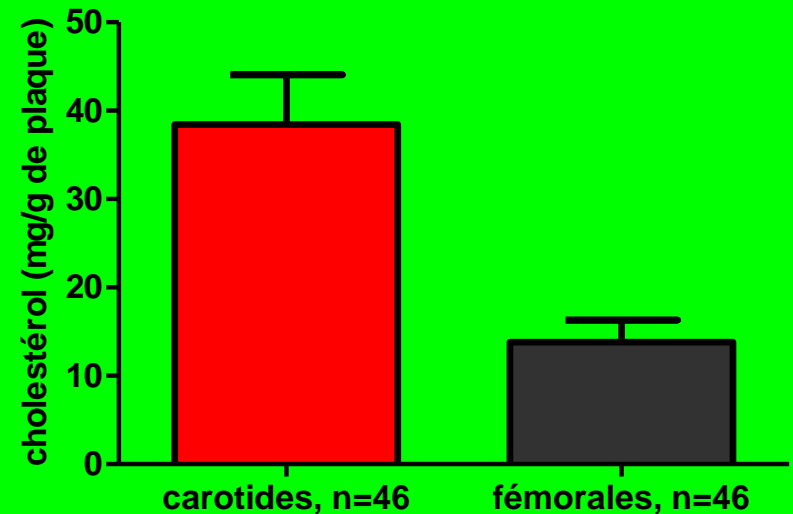
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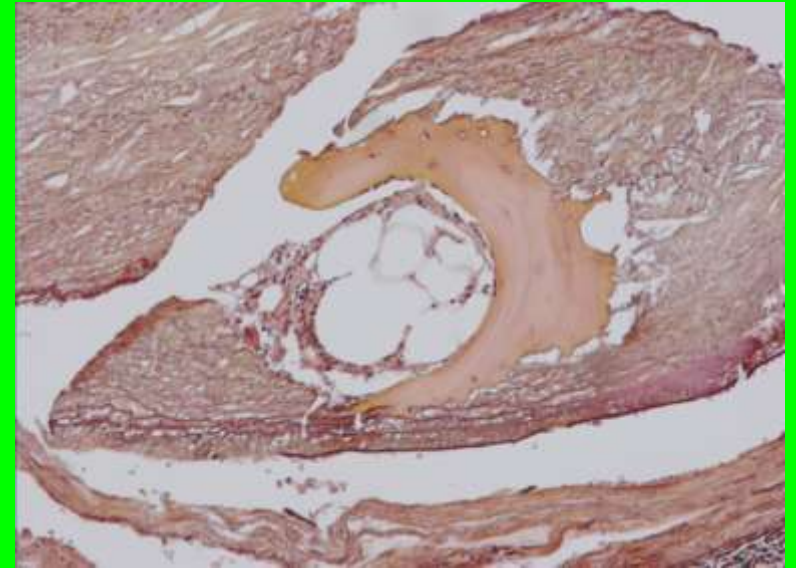
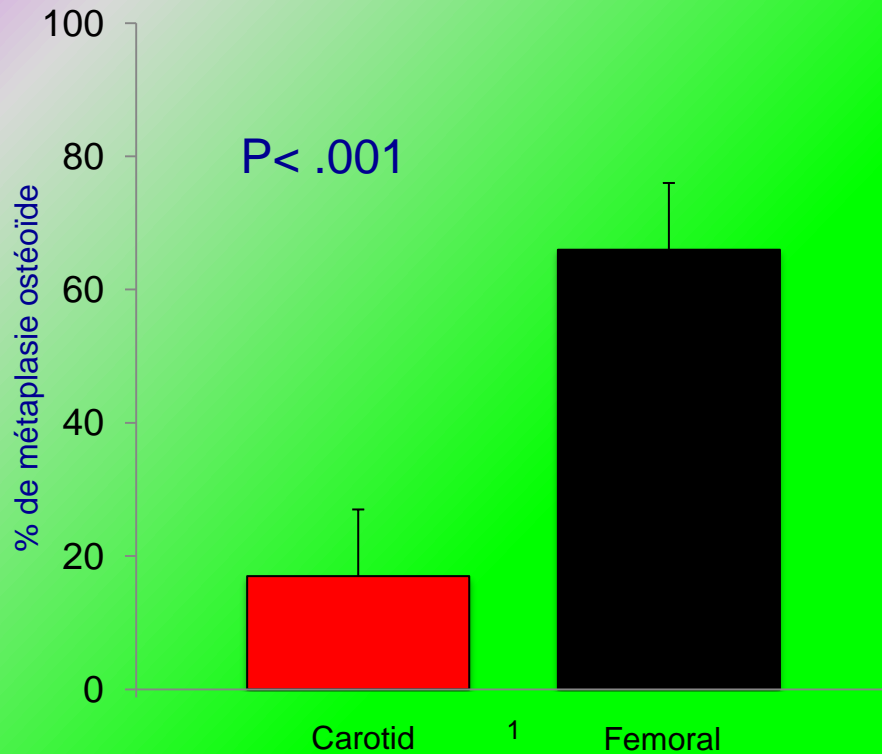
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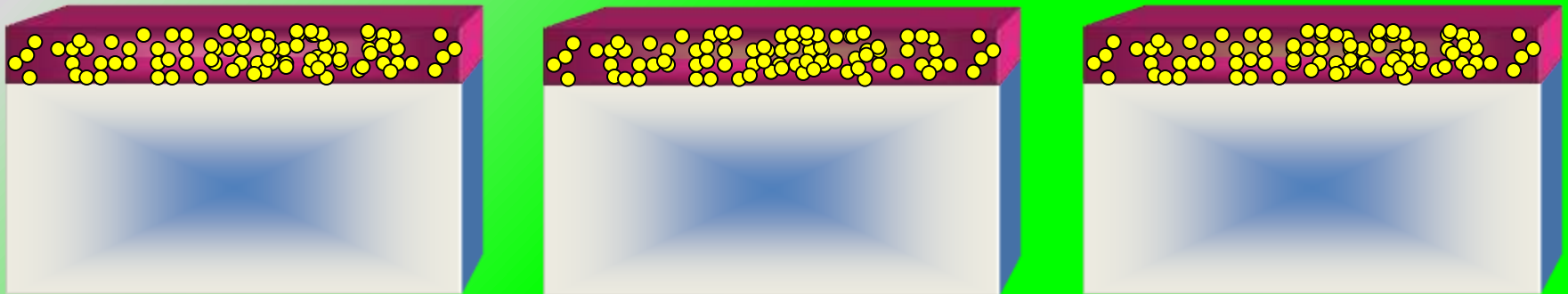
Métaplasie ostéoïde



Hérisson et al, submitted



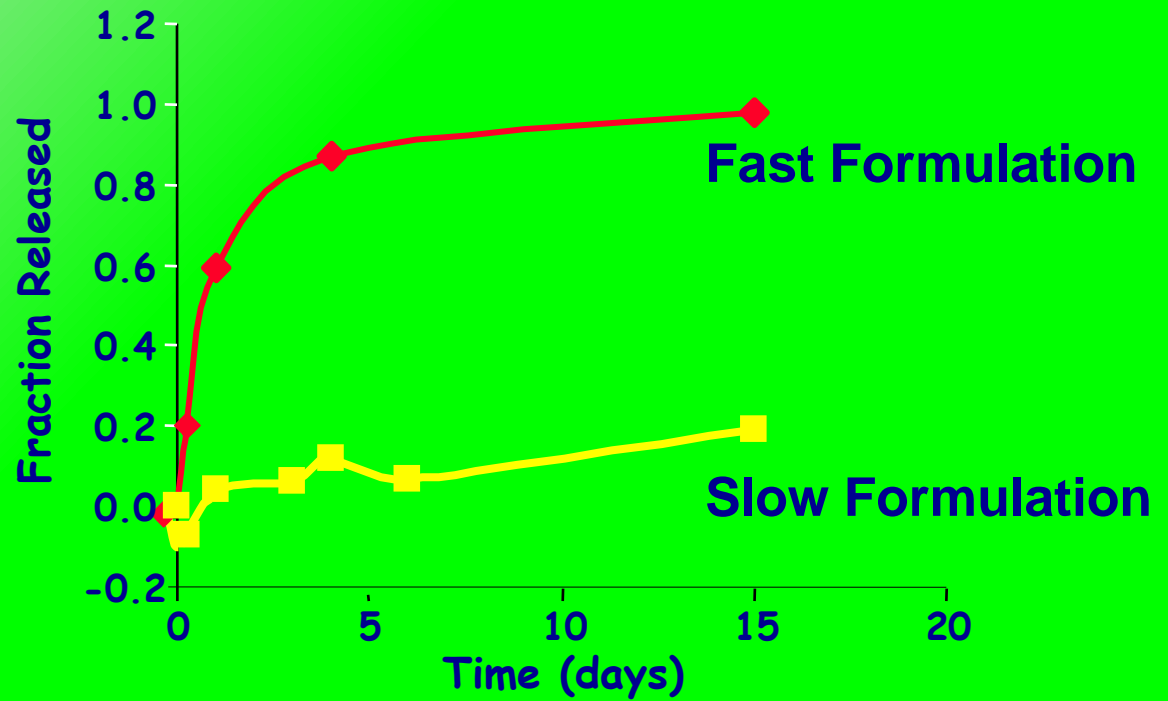
Diffusion controlled matrix system



EVAl polymère



Polymère et relargage



Patient Demographics and Comorbidities

	PTA	Zilver PTX	P-value
Patients	238	236	
Age (years)	68 ± 11	68 ± 10	0.88
Male	64%	66%	0.70
Height (in)	66 ± 4	67 ± 4	0.55
Weight (lbs)	179 ± 44	180 ± 40	0.62
Diabetes	42%	49%	0.13
High cholesterol	70%	76%	0.12
Hypertension	82%	89%	0.02*
Past/current smoker	84%	86%	0.70

* Statistically significant

Baseline Lesion Characteristics

	PTA	Zilver PTX	P-value	
Lesions	251	247		
Normal-to-normal lesion length (mm)	63 ± 41	66 ± 39	0.35	
Stenosed lesion length (mm)^{1,2}	53 ± 40	54 ± 41	0.76	
Diameter stenosis (%)¹	78 ± 17	80 ± 17	0.44	
Total occlusions	25%	30%	0.20	
<i>De novo</i> lesions	94%	95%	0.69	
Lesion calcification¹	None	5%	2%	< 0.01*
	Little	38%	26%	
	Moderate	22%	35%	
	Severe	35%	37%	

¹Angiographic core lab assessment

²Region with > 20% diameter stenosis