

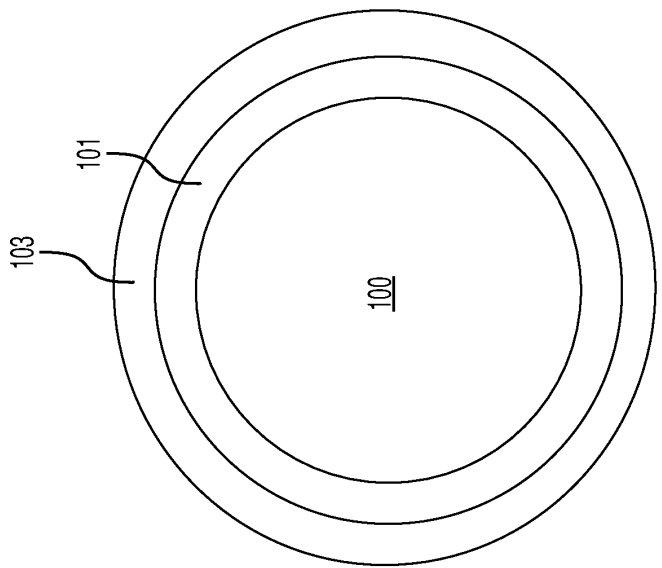


FIG. 1A

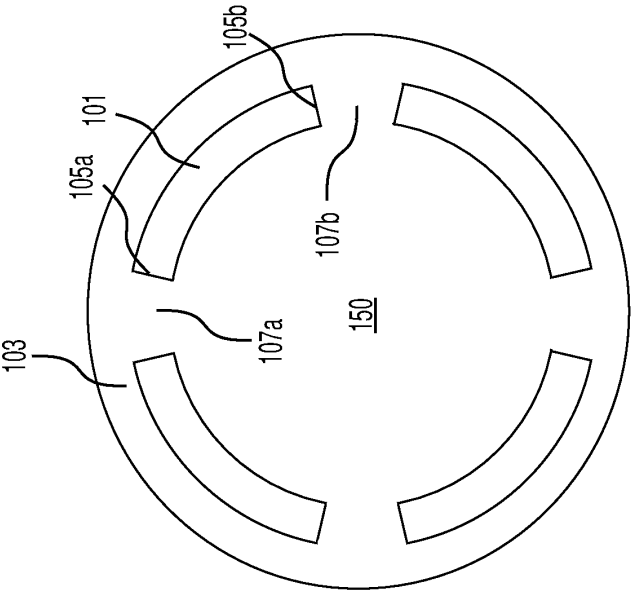


FIG. 1B

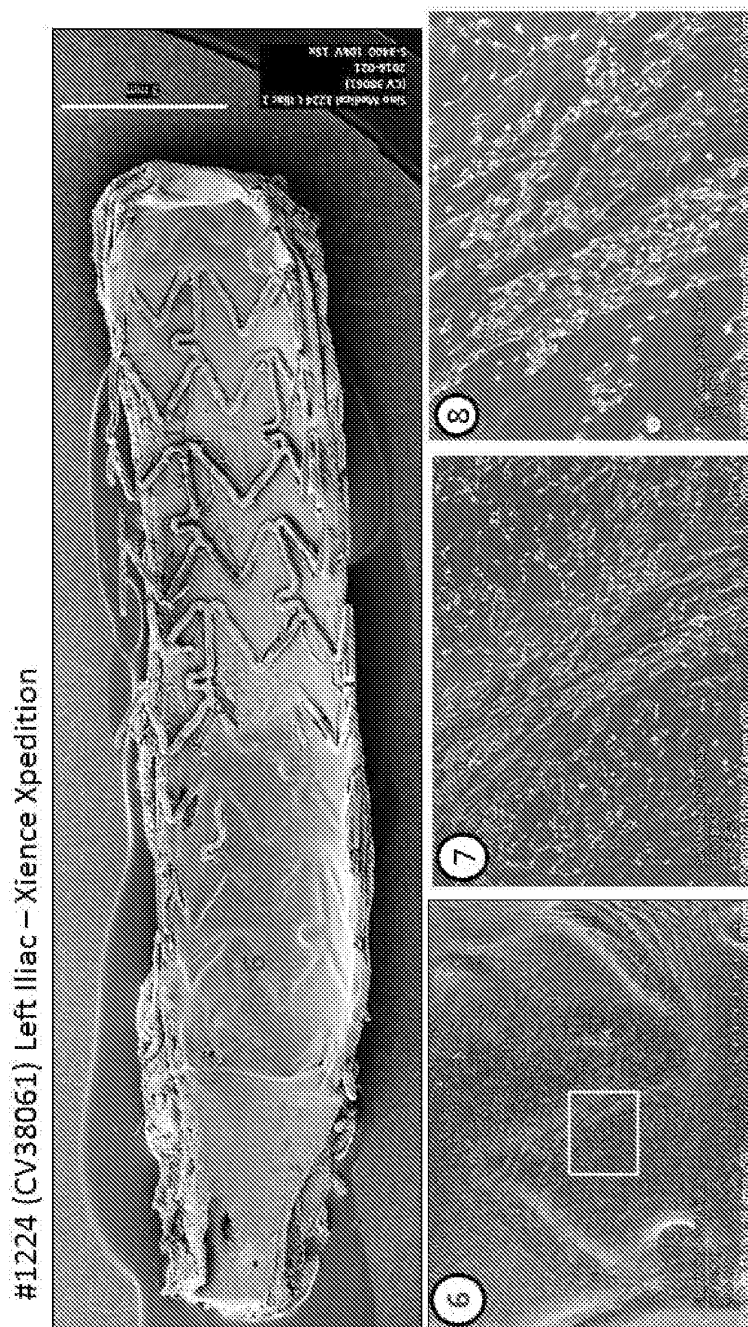


FIG. 2

#1224 (CV38061) Right iliac – BuMA Supreme

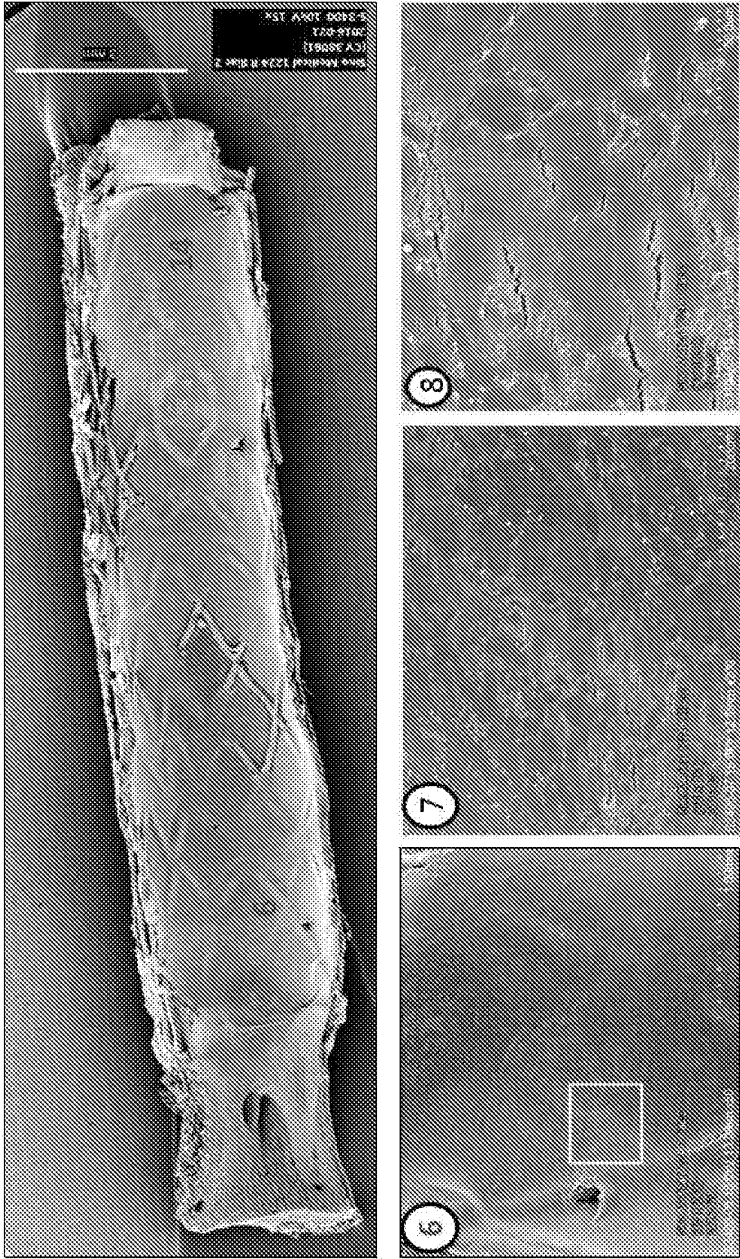


FIG. 3

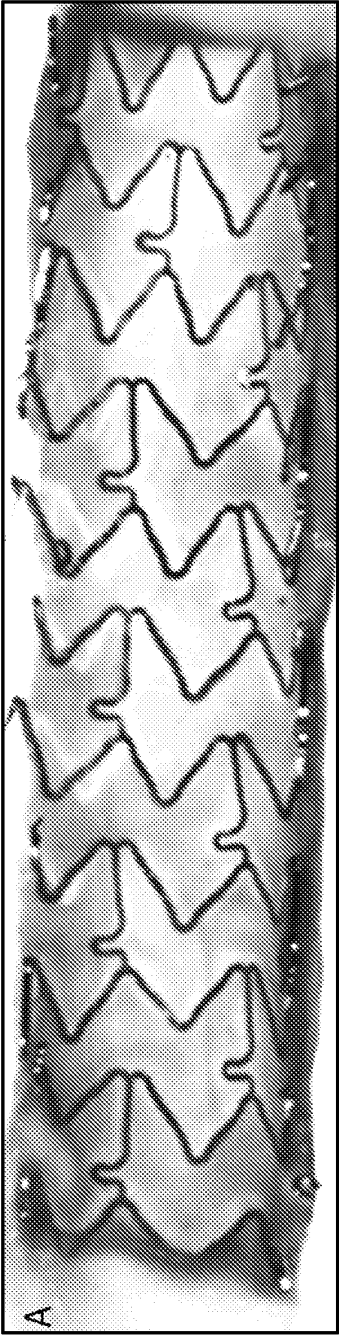


FIG. 4A



FIG. 4B

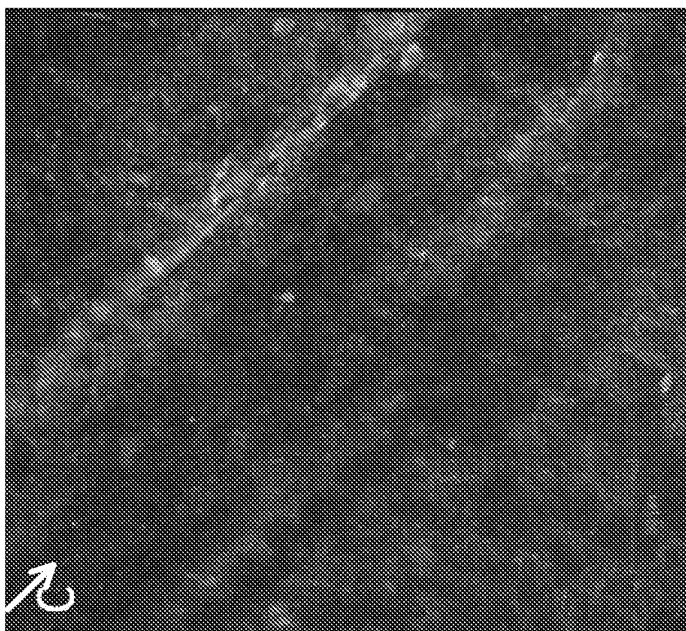


FIG. 4C



FIG. 4D

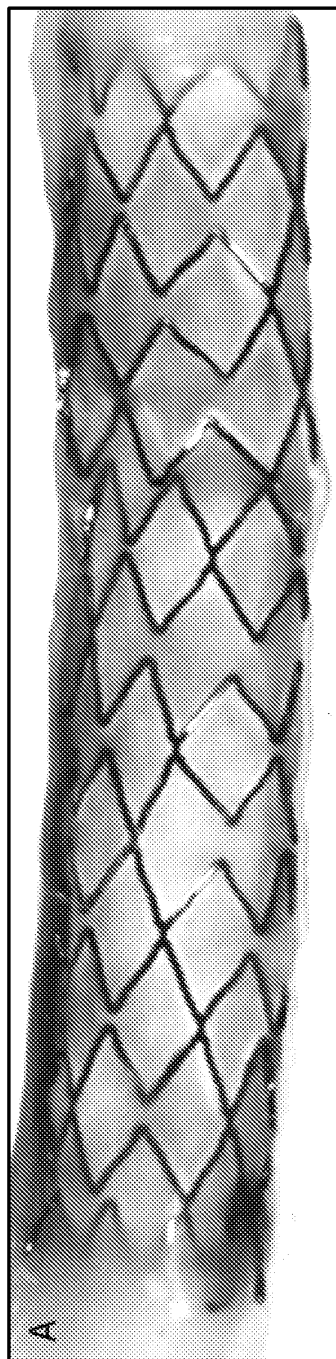


FIG. 5A

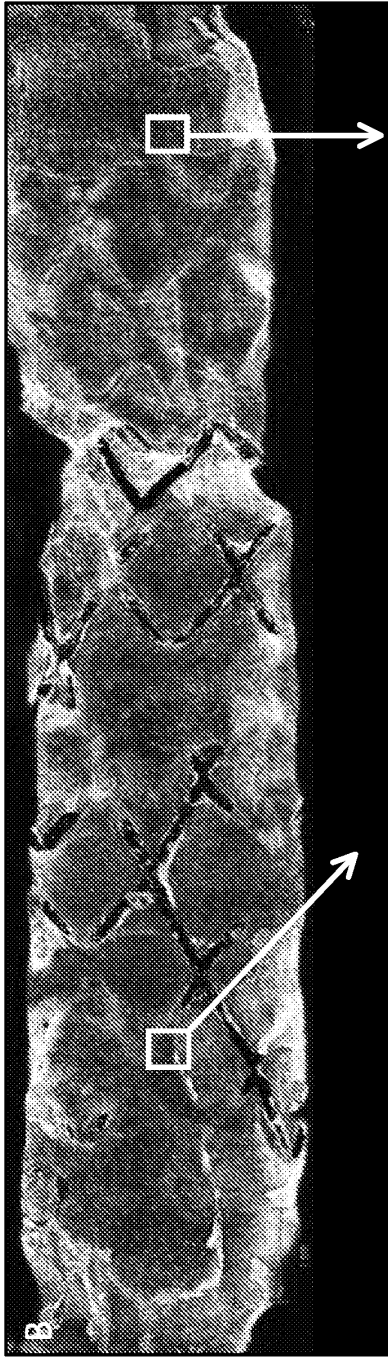


FIG. 5B

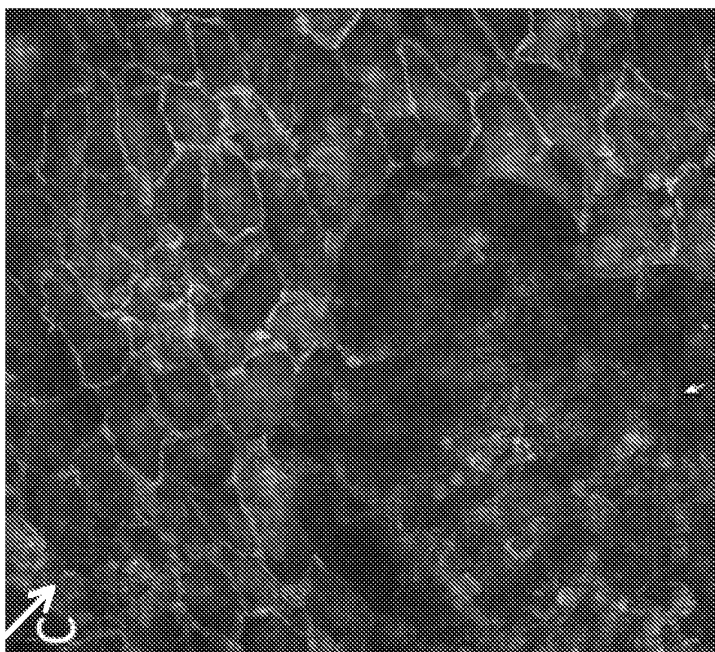


FIG. 5C

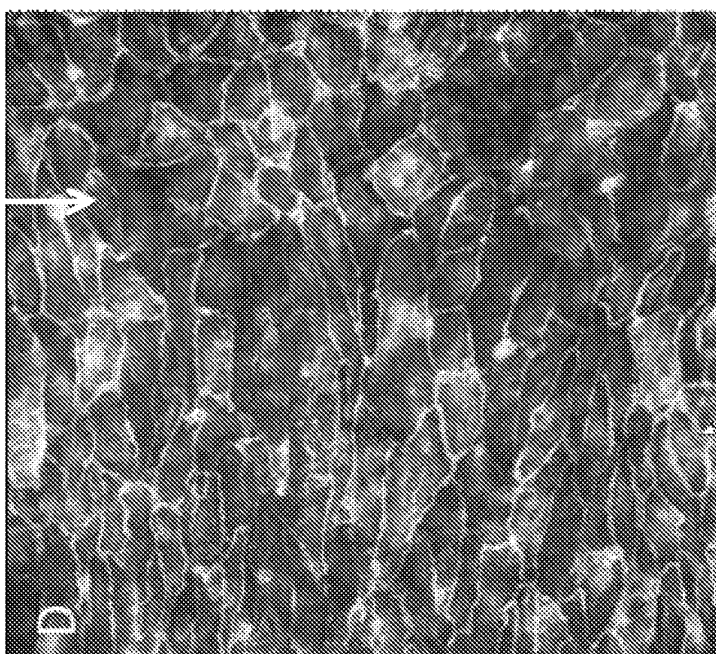


FIG. 5D

#1227 (CV38232) Right Iliac – Xience Xpedition

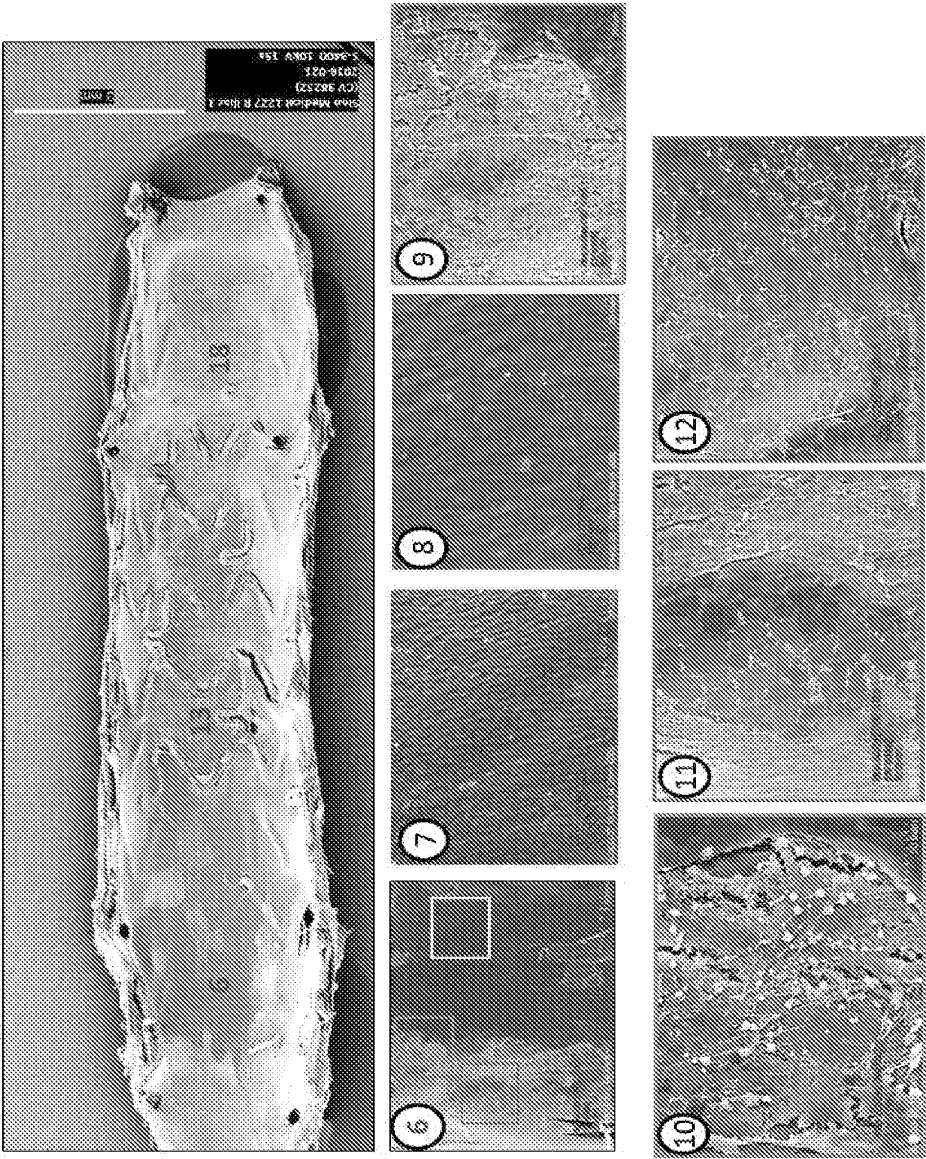


FIG. 6

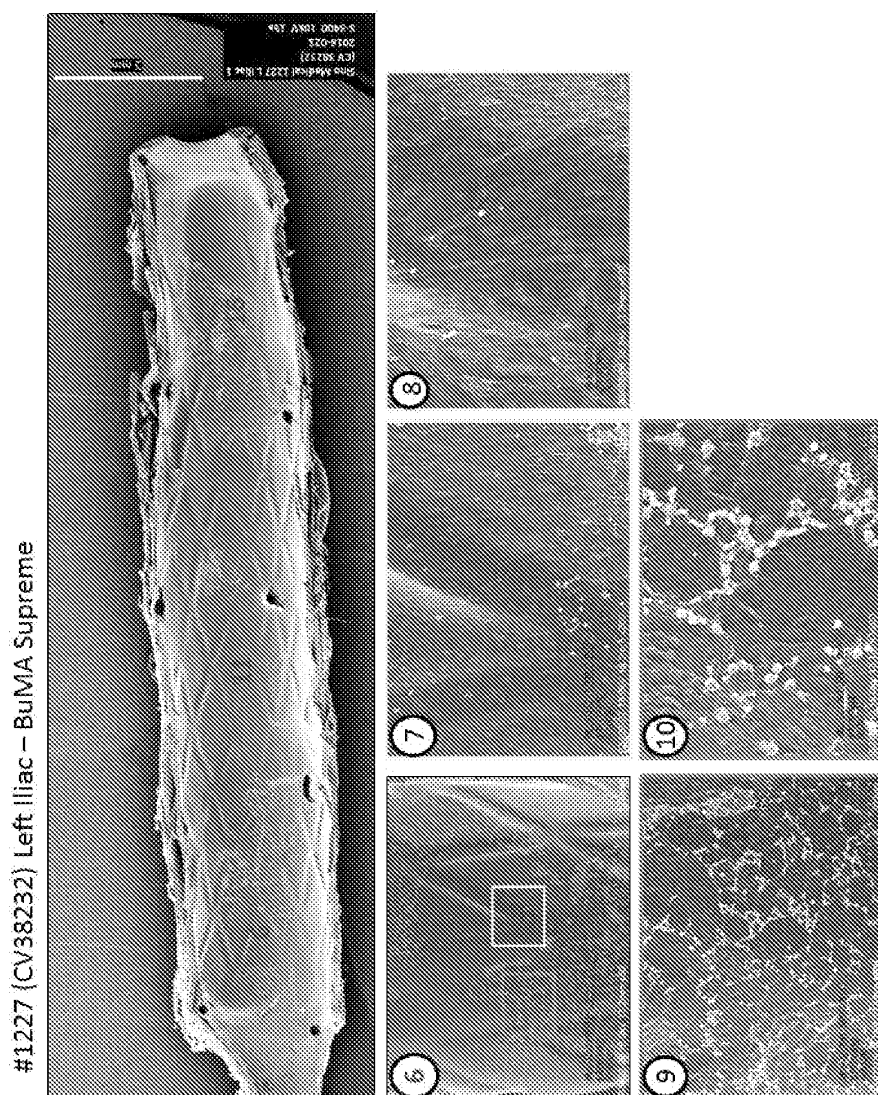


FIG. 7

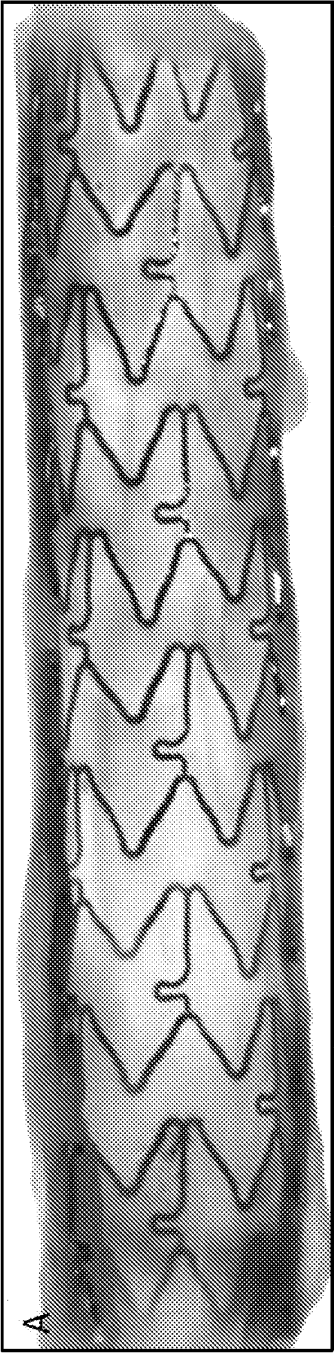


FIG. 8A

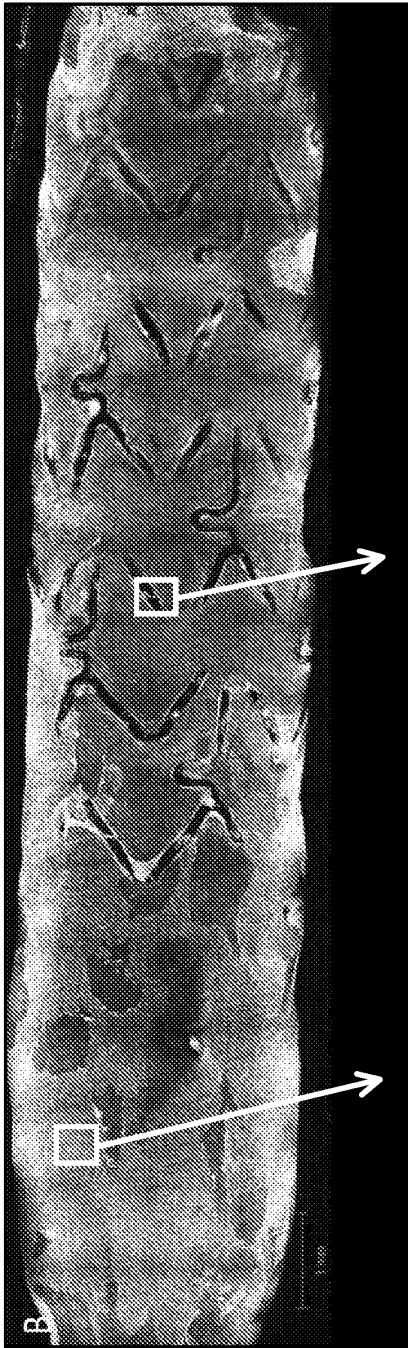


FIG. 8B

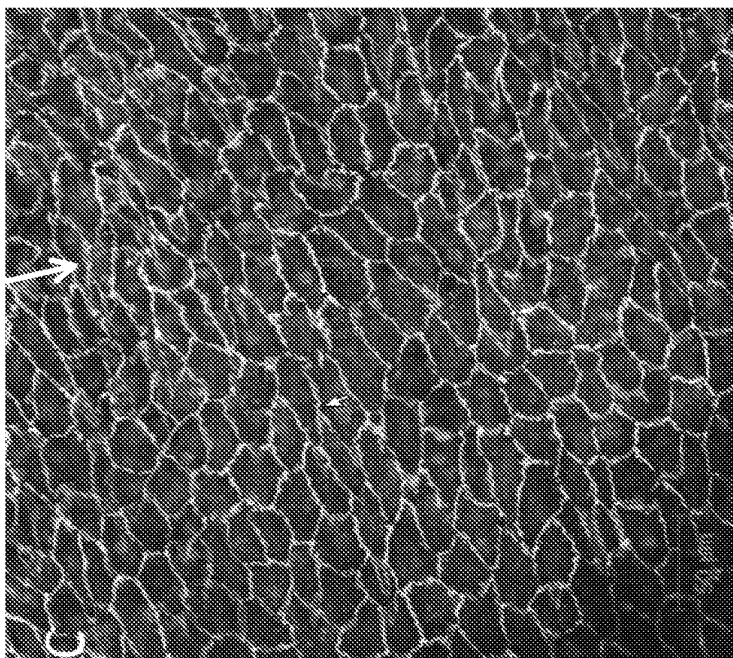


FIG. 8C

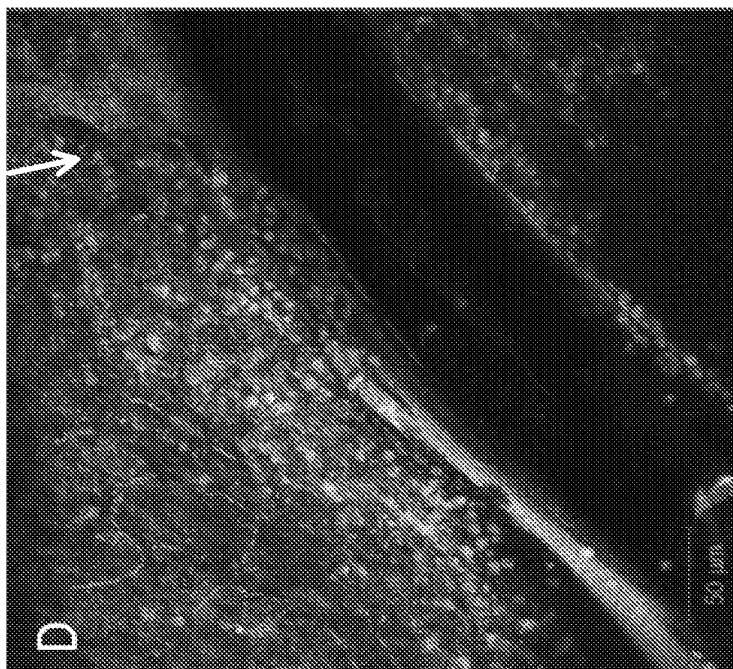


FIG. 8D

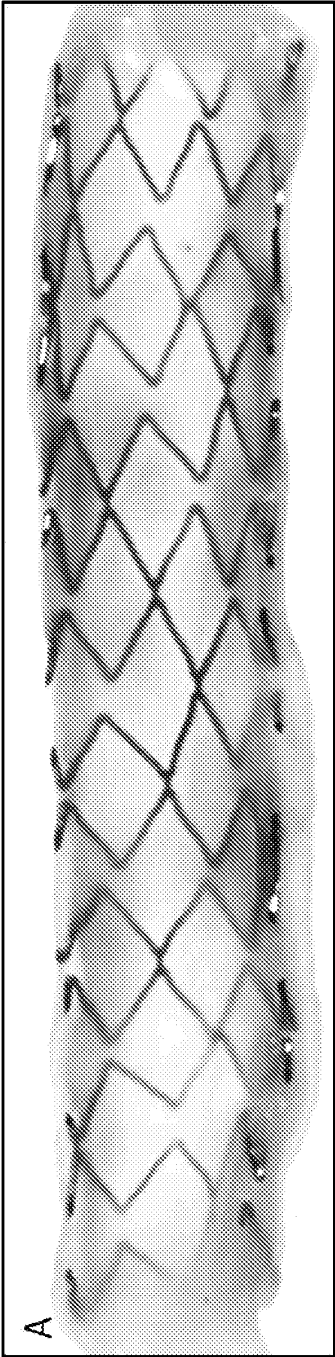


FIG. 9A



FIG. 9B

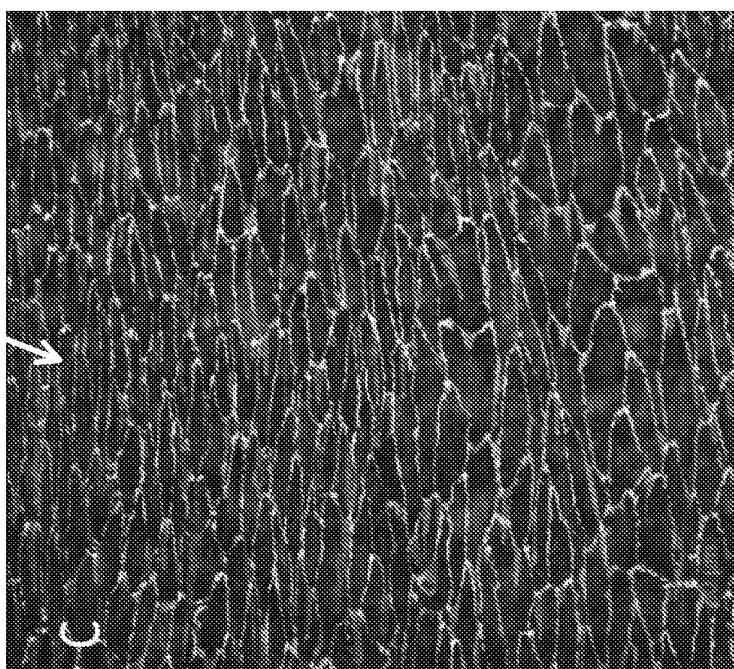


FIG. 9C

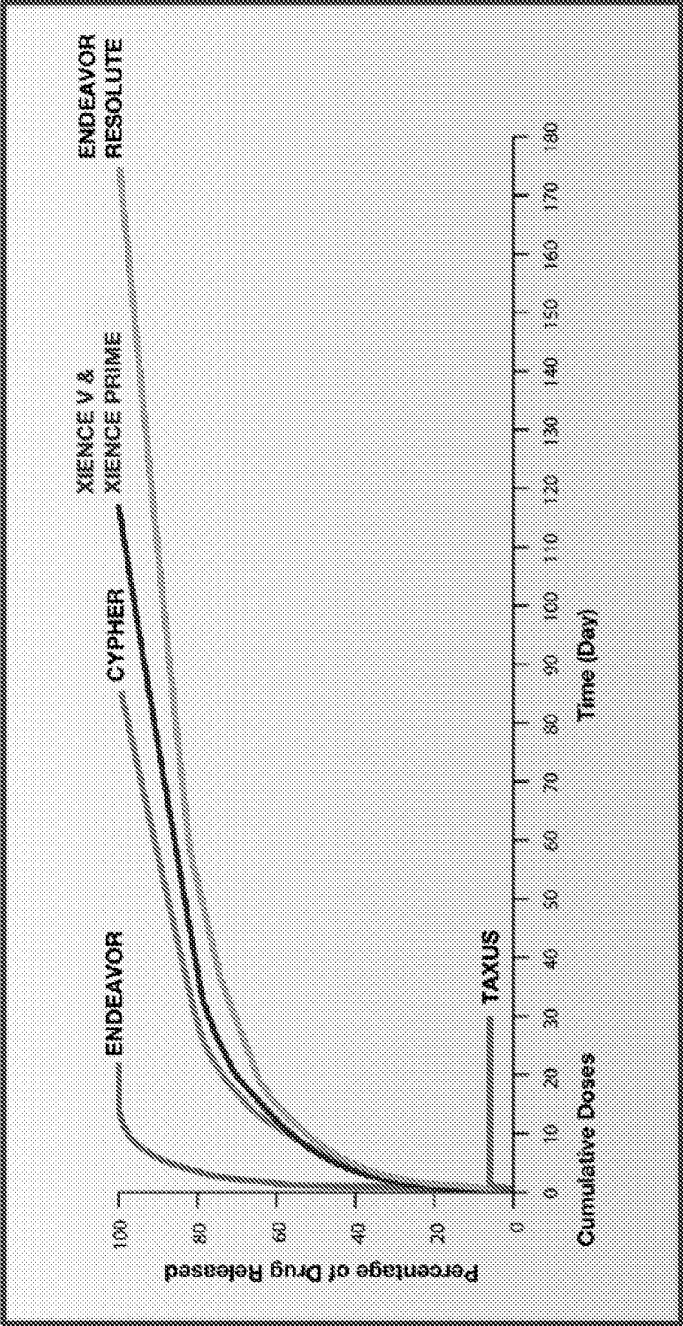


FIG. 10

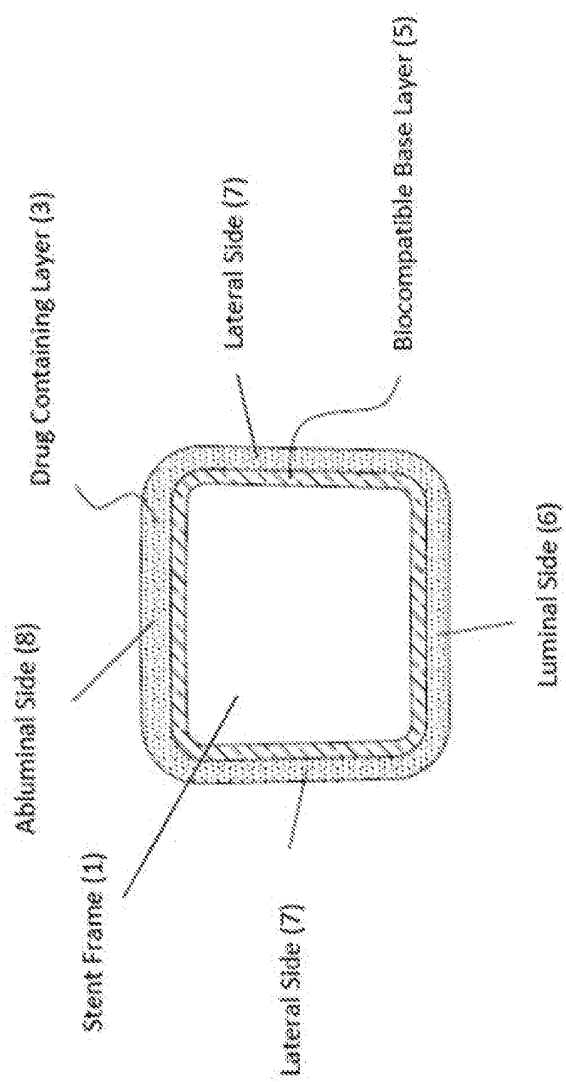


FIG. 11

GROSS IMAGES OF EVAN'S BLUE UPTAKE

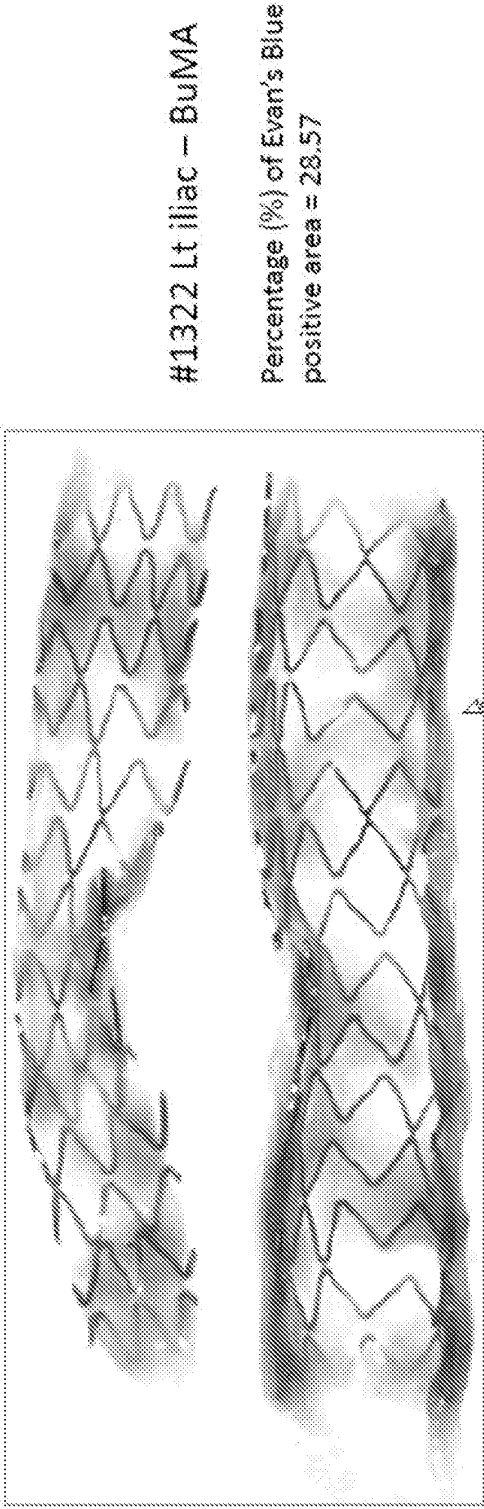
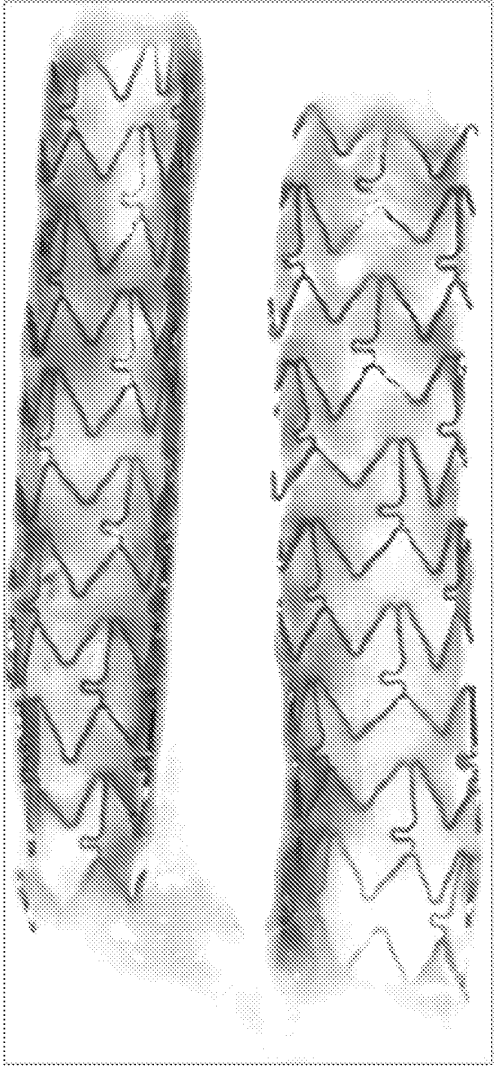


FIG. 12A

GROSS IMAGES OF EVAN'S BLUE UPTAKE

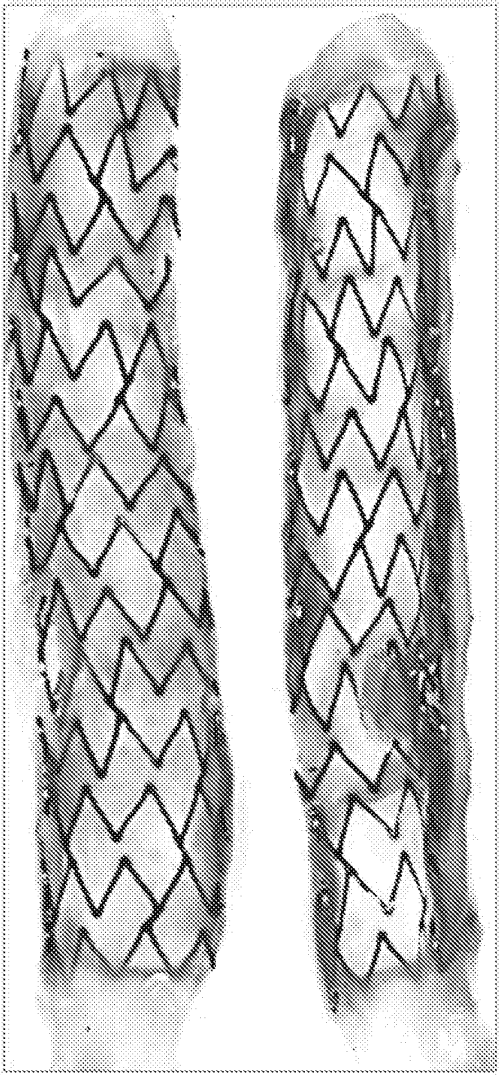


#1324 Lt iliac – Xience

Percentage (%) of Evan's Blue
positive area = 55.0

FIG. 12B

GROSS IMAGES OF EVAN'S BLUE UPTAKE



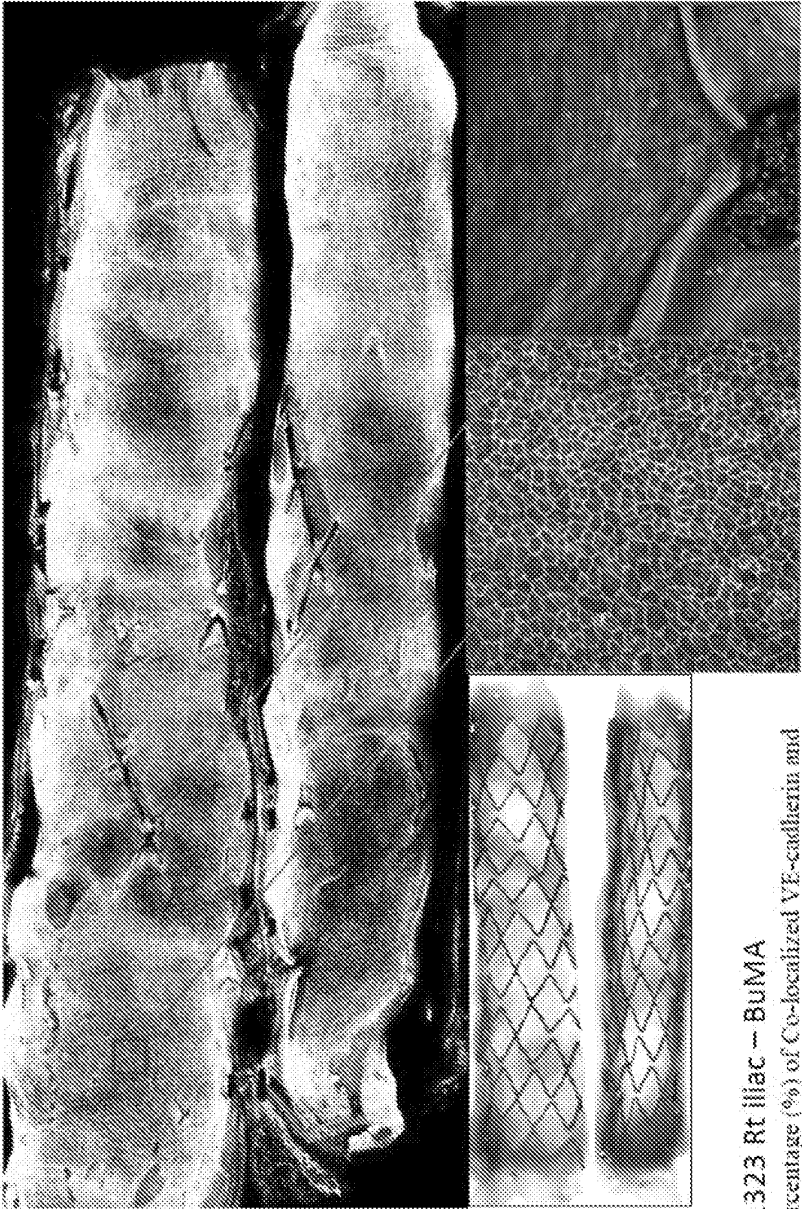
#1325 Lt iliac – Synergy
Percentage (%) of Evan's Blue
positive area = 56.79

FIG. 12C

45 Day Evans Blue
Evan's Blue Uptake Data

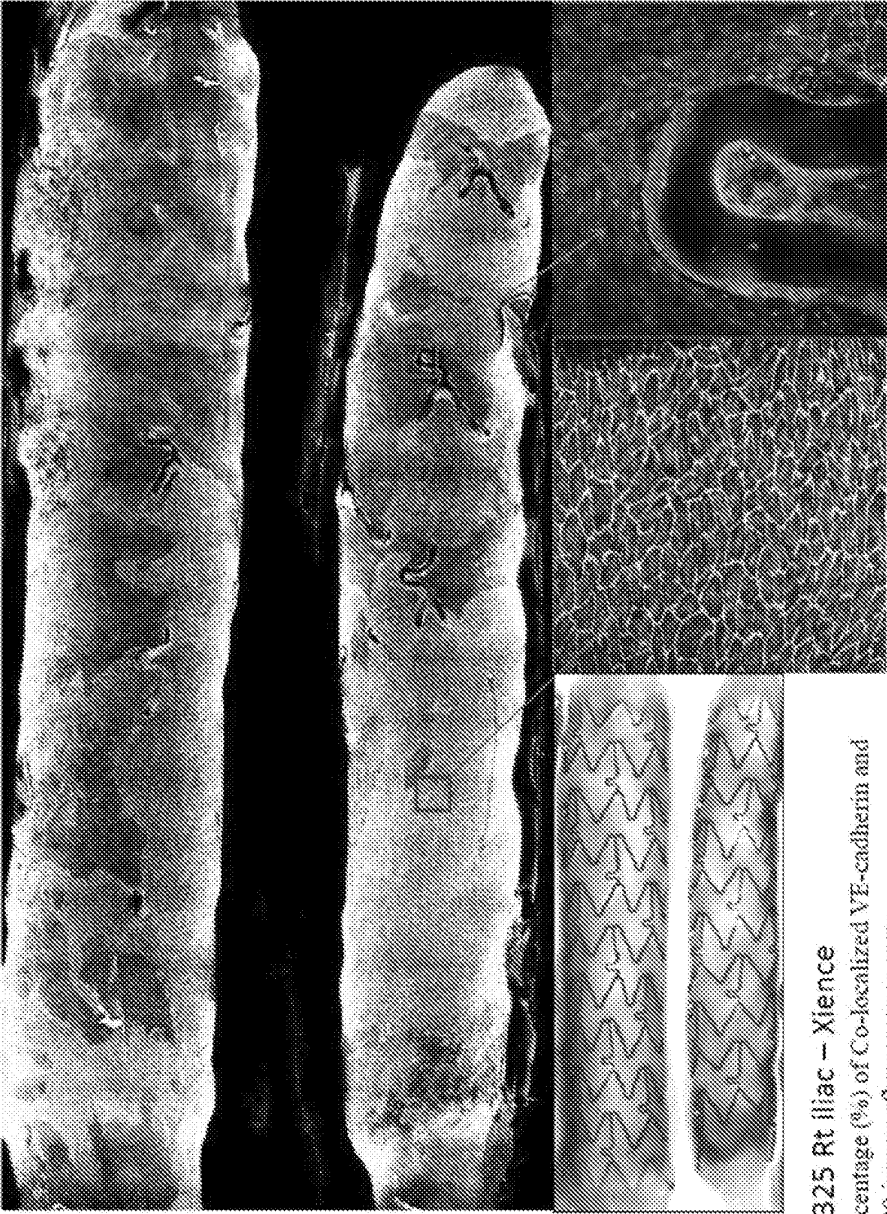
Stent Type	Combined stent halves [Evan's Blue Uptake %]
BuMA Supreme N = 5	35.36 ± 15.91
Xience N = 4	54.71 ± 1.74
Synergy N = 5	42.84 ± 13.93
Vision N = 4	11.2 ± 12.09

FIG. 12D



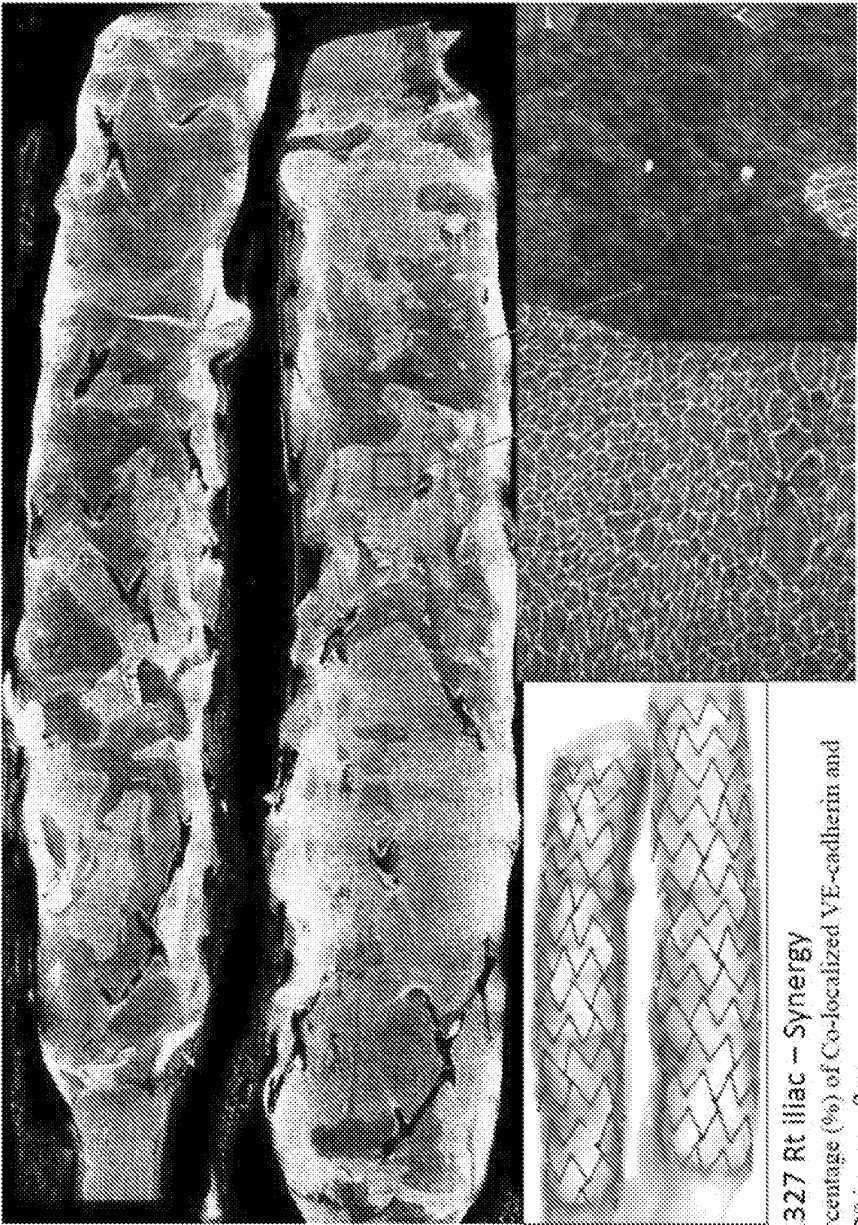
#1323 Rt iliac — BuMA
Percentage (%) of Co-localized VE-cadherin and
P120 immunofluorescence area:
Above Strut = 83.42, Between Strut = 83.08.
Percentage (%) of Evan's Blue positive area = 38.39

FIG. 13A



#1325 Rt iliac – Xience
Percentage (%) of Co-localized VE-cadherin and
P120 immunofluorescence area:
Above Strut = 48.37, Between Strut = 48.14.
Percentage (%) of Evan's Blue positive area = 55.23

FIG. 13B



#1327 Rt iliac – Synergy
Percentage (%) of Co-localized VE-cadherin and
P120 immunofluorescence area:
Above Strut = 27.17, Between Strut = 39.54,
Percentage (%) of Evan's Blue positive area = 40.18

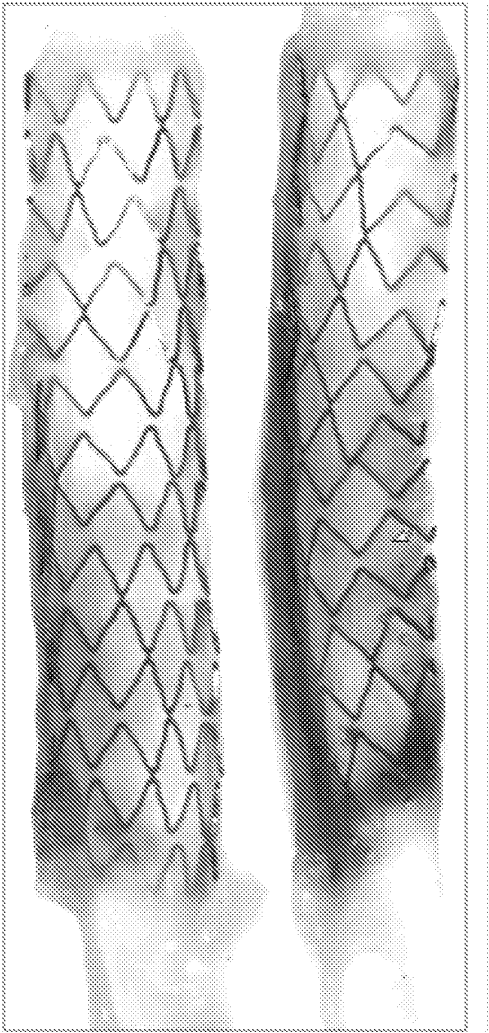
FIG. 13C

45 Day VE-cadherin
VE-Cadherin and P120 Immunofluorescence Staining

Percentage of EC Barrier Protein Expression			
Stent Type	Above Struts	P Value	Between Struts
BuMA Supreme N = 5	60.77 ± 34.46	0.014	59.35 ± 34.27
Xience N = 4	37.09 ± 21.88		36.46 ± 20.7
Synergy N = 5	42.99 ± 23.75		46.29 ± 24.39
Vision N = 4	97.81 ± 3.74		98.07 ± 2.88

FIG. 13D

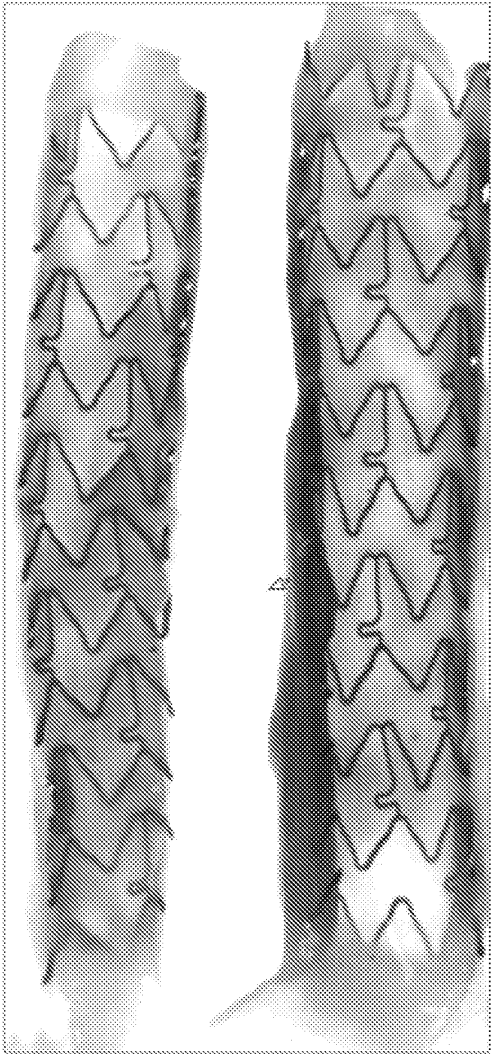
GROSS IMAGES OF EVAN'S BLUE UPTAKE



#1313 Rt Iliac – BuMA
Percentage (%) of Evan's Blue
positive area = 23.21

FIG. 14A

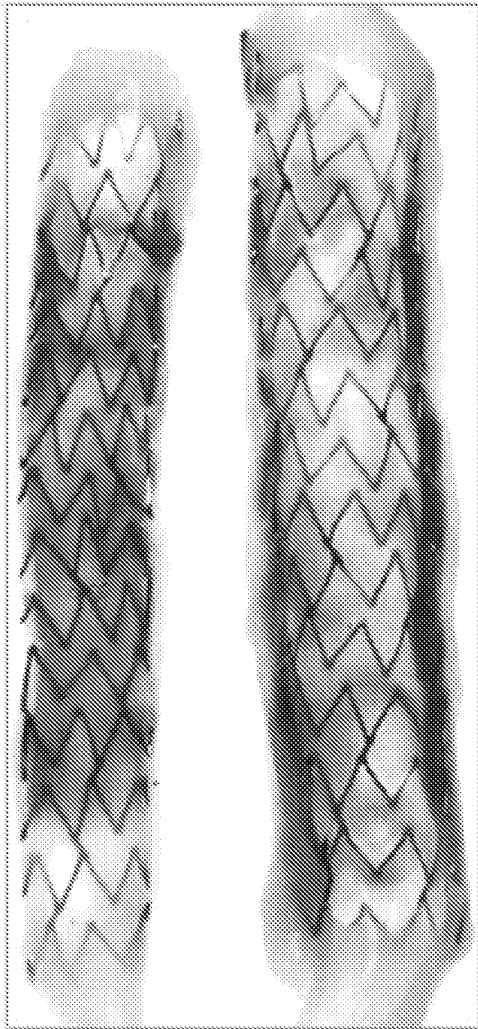
GROSS IMAGES OF EVAN’S BLUE UPTAKE



#1313 Lt iliac – Xience
Percentage (%) of Evan's Blue
positive area = 42.95

FIG. 14B

GROSS IMAGES OF EVAN’S BLUE UPTAKE



#1314 Rt iliac – Synergy
Percentage (%) of Evan's Blue
positive area = 41.79

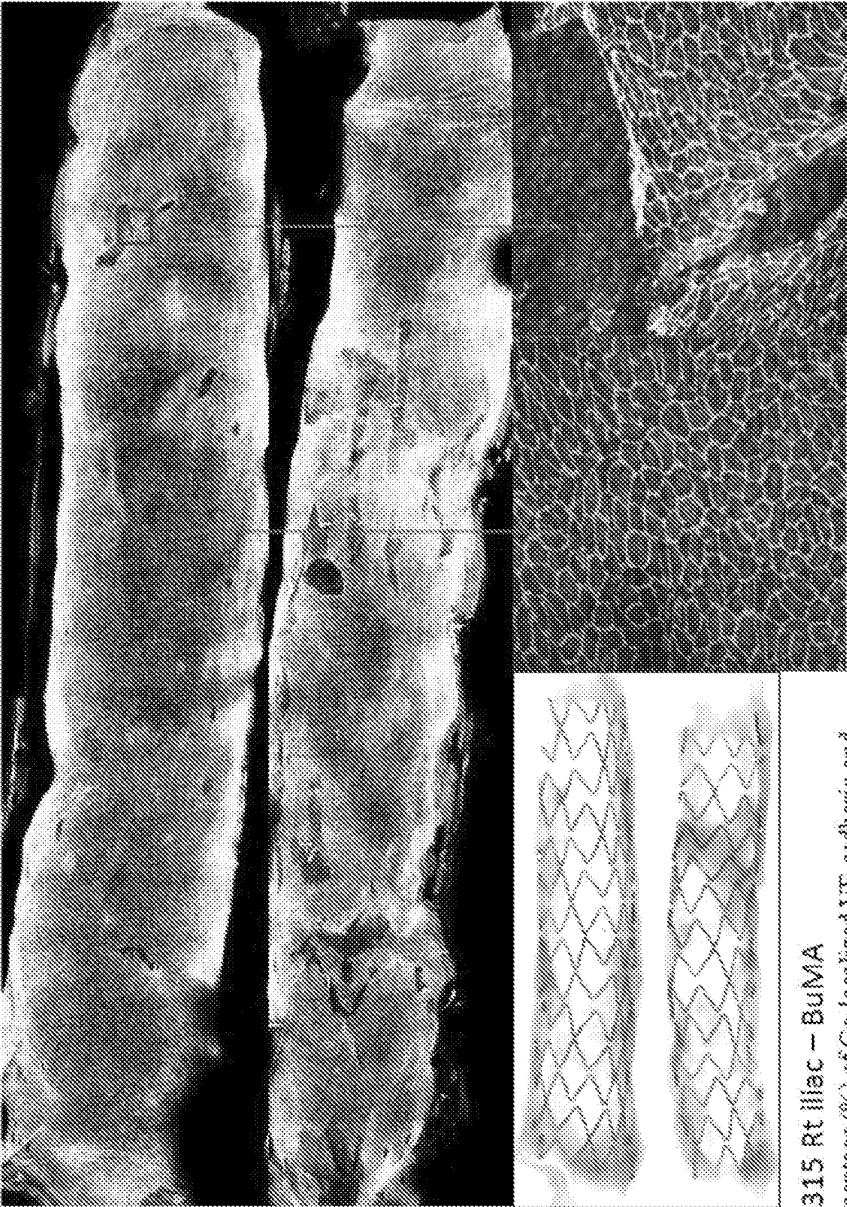
FIG. 14C

Assessment of Endothelial Barrier Function – Evan’s Blue Uptake

Table 3. Mean percentage (%) of Evan’s Blue positive area by visual examination from both stent halves, normalized to total stented area (90 days)

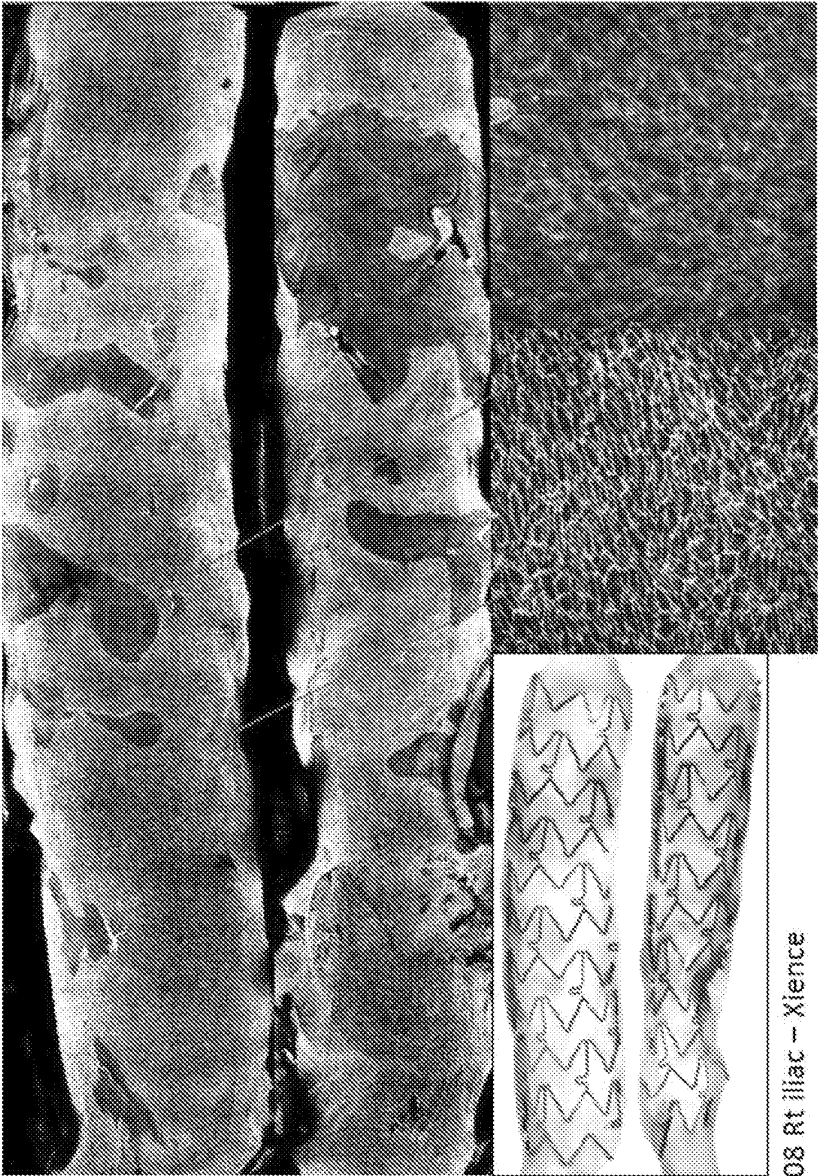
Stent Type	Combined stent halves [Evan’s Blue Uptake %]
BuMA Supreme N = 6	22.89 ± 8.25
Xience N = 5	39.41 ± 12.5
Synergy N = 5	31.11 ± 20.62
Vision N = 6	6.6 ± 4.67

FIG. 14D



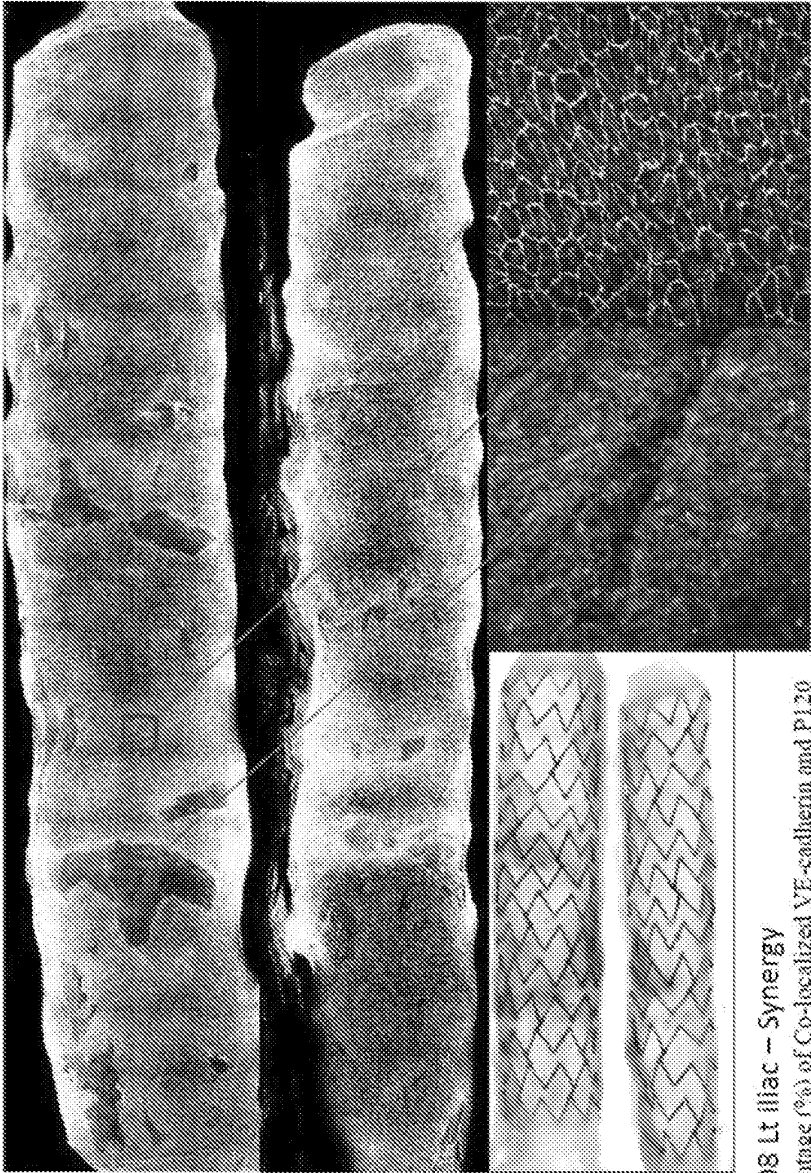
#1315 Rt Iliac – BuMA
Percentage (%) of Co-localized VE-cadherin and
P120 immunofluorescence area:
Above Strut = 98.78, Between Strut = 98.58,
Percentage (%) of Evan's Blue positive area = 10.0

FIG. 15A



#1308 Rt iliac – Xience
Percentage (%) of Co-localized VE-cadherin and P120 immunofluorescence area:
Above Strut = 79.7, Between Strut = 79.95,
Percentage (%) of Evan's Blue positive area = 18.18

FIG. 15B



#1308 Lt Iliac – Synergy
Percentage (%) of Co-localized VE-cadherin and P120
immunofluorescence area:
Above Strut = 95.07, Between Strut = 95.34,
Percentage (%) of Evan's Blue positive area = 6.96

FIG. 15C

Dual IHC for Endothelial Coverage with Confocal Microscopy Analysis

Assessment Endothelial Cell Barrier Function by VE-cadherin and P120
Immunofluorescence Staining (90 days)

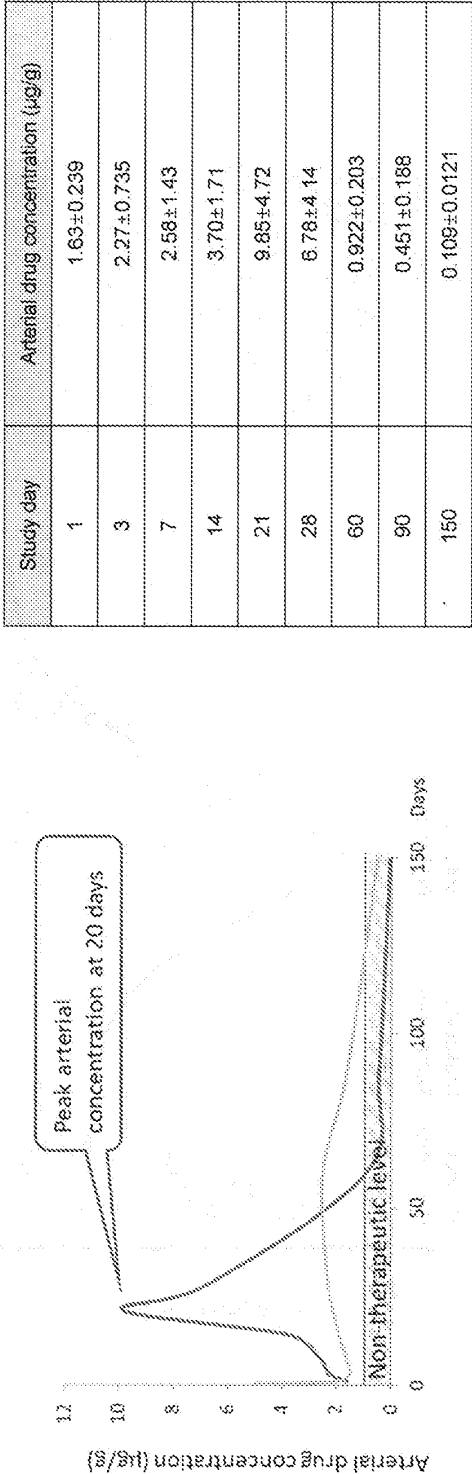
Table 3. Mean percentage (%) of Co-localized VE-cadherin and P120 immunofluorescence area (µm2) above and between struts relative to total stented area (µm2). Data collected from both halves of each stent

	Percentage of EC Barrier Protein Expression	
Stent Type	Above Struts	Between Struts
BuMA Supreme N = 6	82.54 ± 20.76	81.56 ± 22.17
Xience N = 5	55.73 ± 24.32	56.38 ± 25.79
Synergy N = 5	80.73 ± 21.62	82.36 ± 20.08

FIG. 15D

FIG. 16A
BuMA has an optimized release kinetic for an arterial peak at 20 days and fast polymer degradation

Arterial Sirolimus Concentration
measured in vivo



Source: Data on file.

FIG. 16B Pharmacokinetics designed to suppress SMC without limiting functional healing

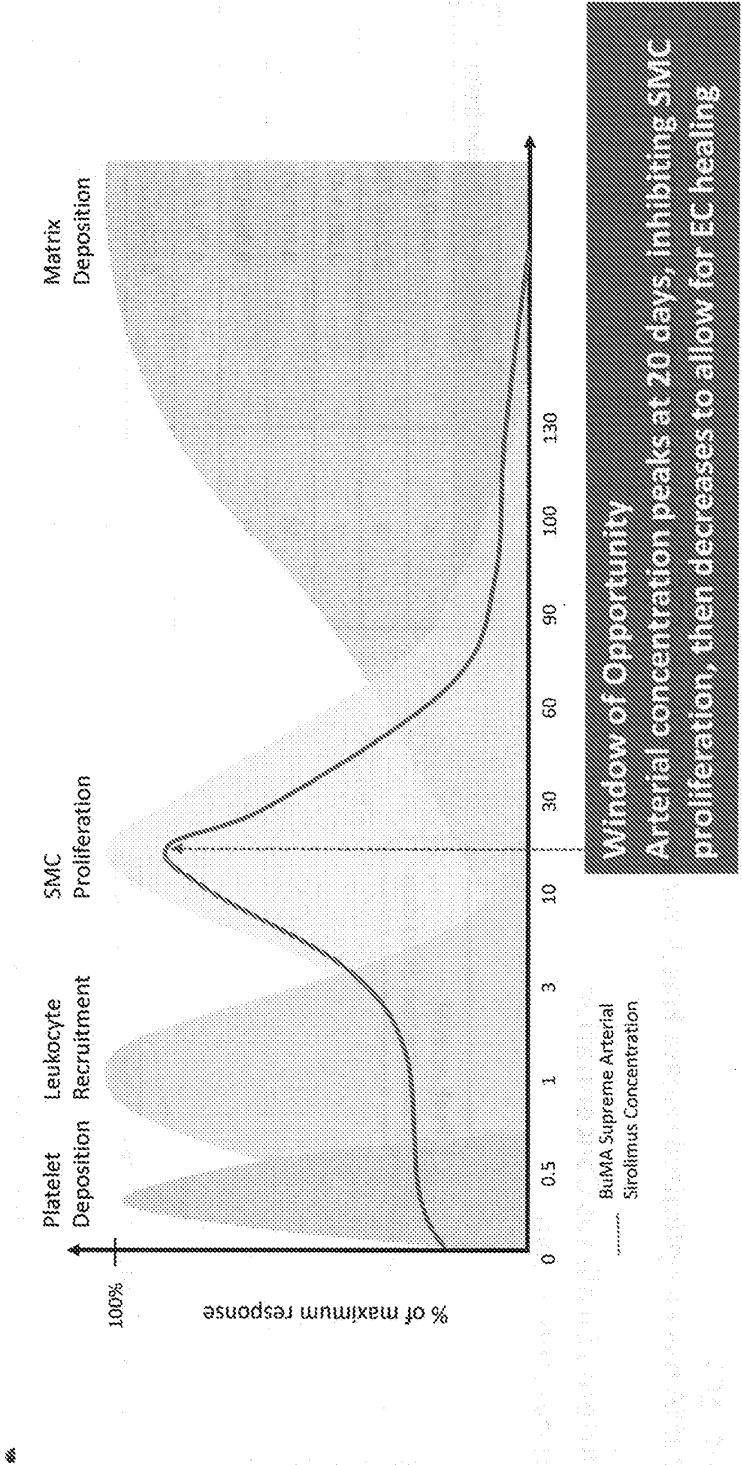
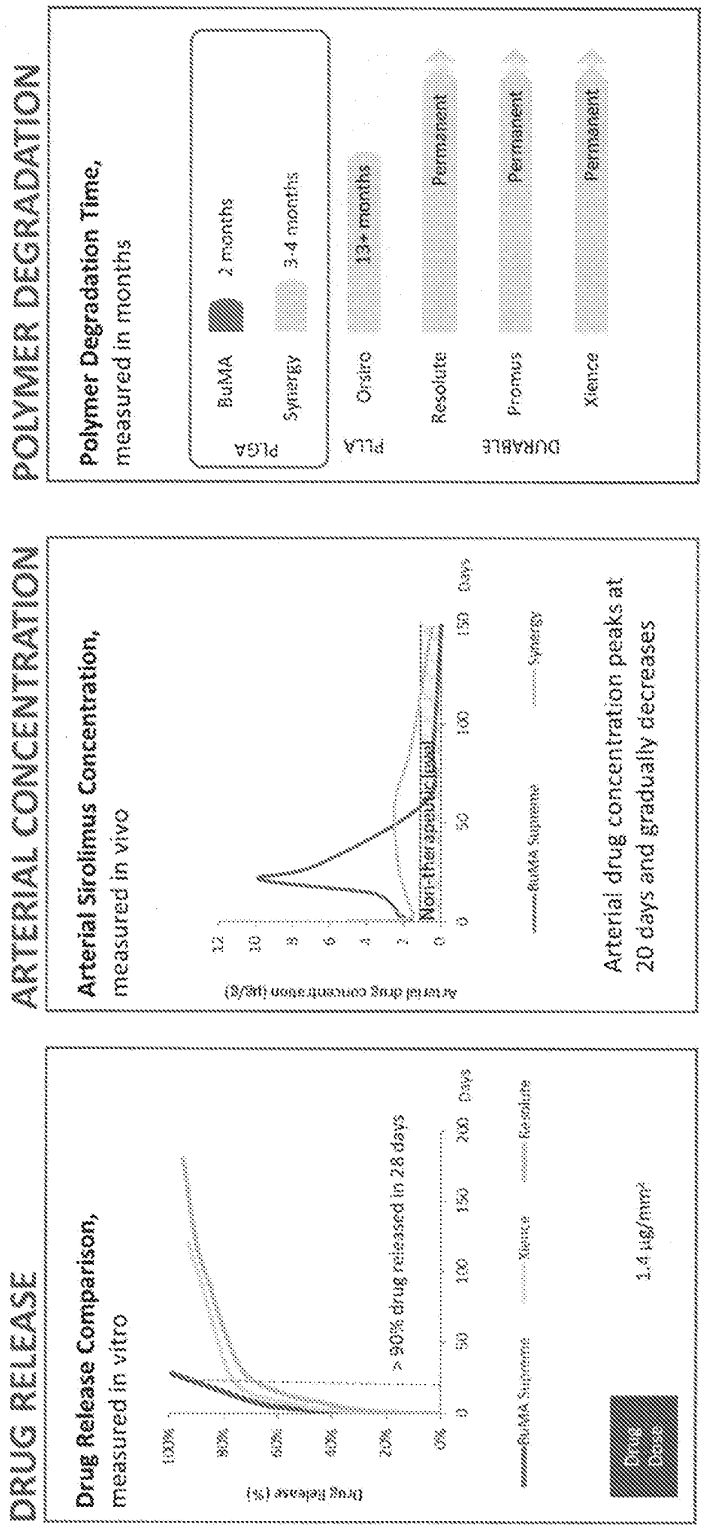


FIG. 16C
BuMA has an optimized pharmacokinetic for a peak in arterial concentrations at 20 days



Source: Data on file.

FIG. 17

Study device characteristics.

Stent	Metal material	Metal thickness	Polymer thickness/coating	Polymer material	Drug	Drug loading dose	Duration of polymer degradation	Duration of drug release
Bulma Supraene® (BP-SES)	CuCr	80 µm	3.8–10 µm /circumferential	PLGA-eG ^a	Sitrolimus	1.2 µg/mm ²	1.5 months ^b	1 month
Xience Xpedition® (DP-EES)	CoCr	81 µm	8 µm /circumferential	PVDF-HFP	Everolimus	1.0 µg/mm ²	Permanent	3–4 months
Symargo® (BP-EES)	PtCr	74 µm	4 µm /abulminal	PLGA	Everolimus	113 µg/20 mm	4 months	3 months
Multilink Vision® (BMS)	CoCr	81 µm	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: BMS = bare metal stent (Multilink Vision®), BP-SES = biodegradable polymer everolimus-eluting stent (Symargo®), BP-SES = biodegradable polymer sitrolimus-eluting stent (Bulma Supraene®), CoCr = cobalt-chromium, DP-EES = durable polymer everolimus-eluting stent (Xience Xpedition®), eG = electro-grafting, N/A = not available, PLGA = poly lactic-co-glycolic acid, PtCr = platinum-chromium, PVDF-HFP = poly vinylidene fluoride-co-hexafluoropropylene.

^a eG is ultra-thin (200 nm) electrografted base layer of poly n-butyl methacrylate (permanent polymer without drug contents) under drug contained PLGA biodegradable polymer.

^b This is for drug containing PLGA polymer.

FIG. 19A-19N

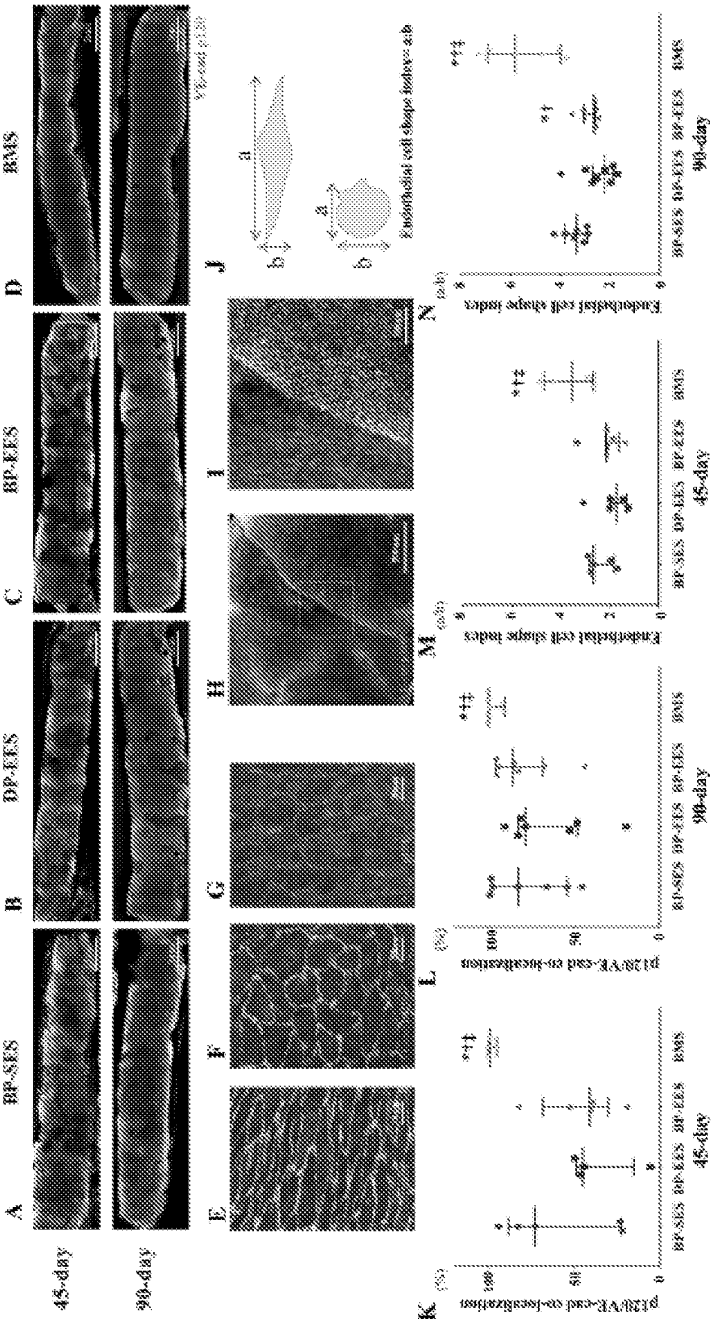


FIG. 20A-20F

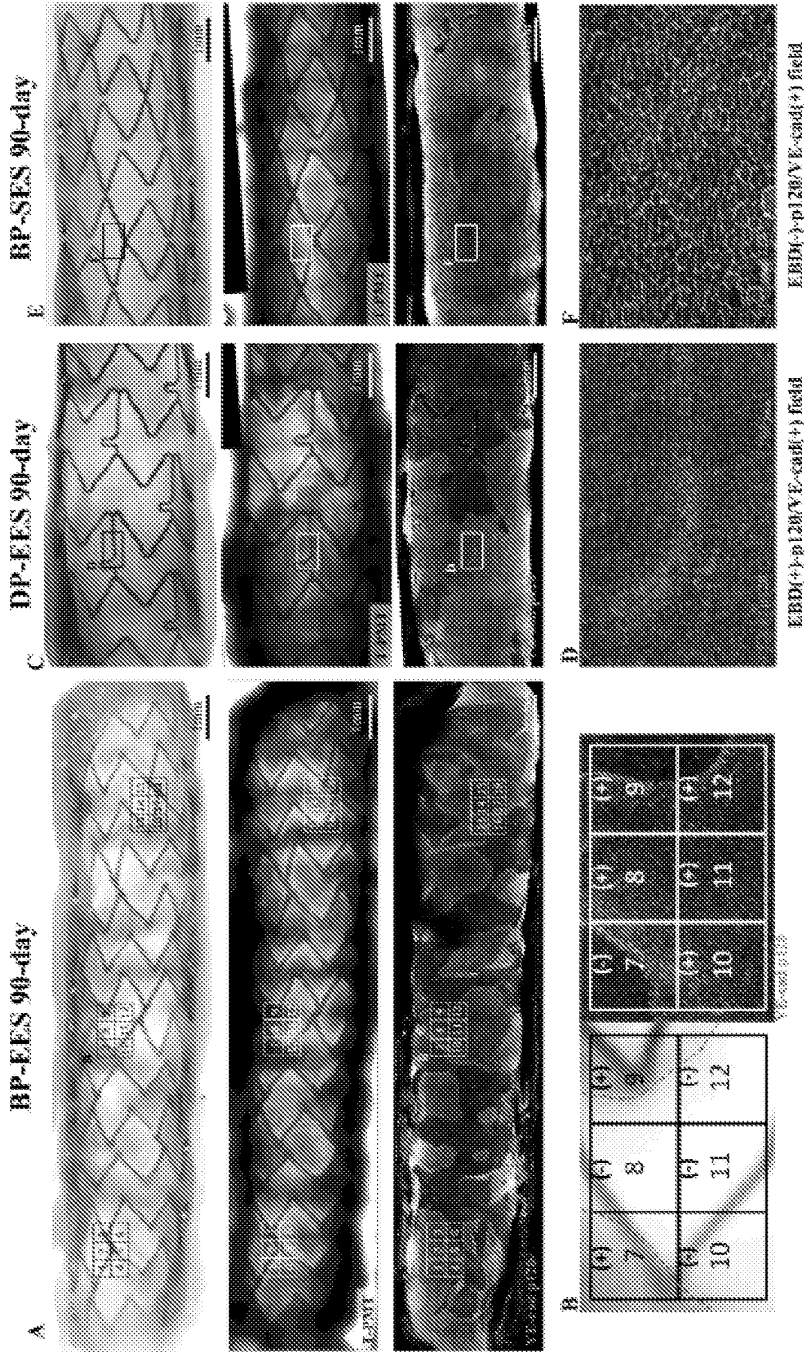


FIG. 21

Comparison of Evans blue dye and p120/VE-cadherin for the detection of endothelial permeability.

	p120/VE-cad (—)	p120/VE-cad (+)	Total	P value
EBD (+)	476 (28.7%)	188 (11.4%)	664 (40.1%)	
EBD (—)	39 (2.4%)	953 (57.5%)	992 (59.9%)	<0.0001
Total	515 (31.1%)	1141 (68.9%)	1656	

Abbreviations: EBD == Evans blue dye, p120/VE-cad == p120/vascular-endothelial cadherin colocalization, (+) == positive, (—) == negative.

FIG. 22A-22N

