Figure 1

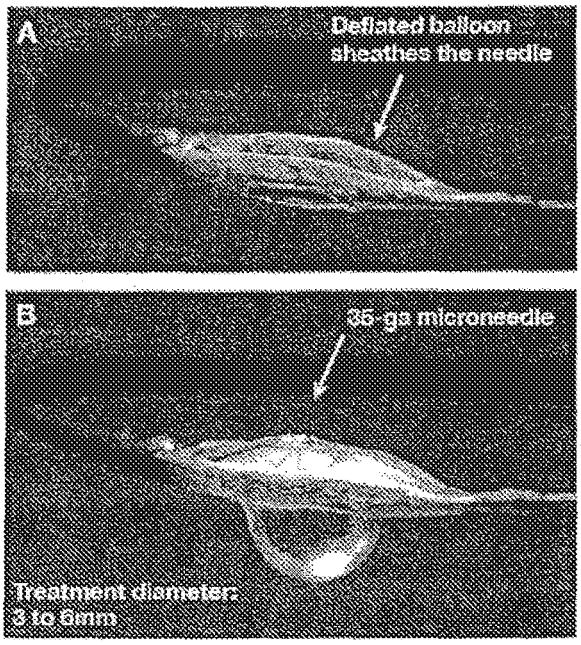
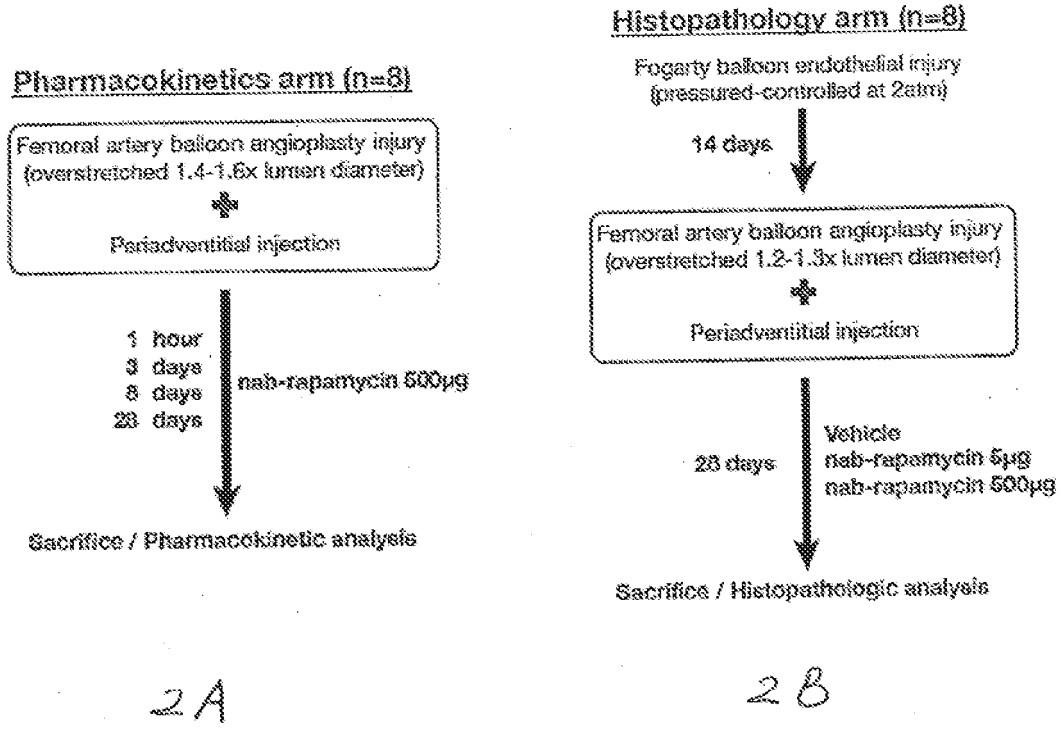

A
Deflated balloon sheathes the needle
B
35 ga microneedle
Treatment diameter: 3 to 6mm

Figure 2



2A 2B

Figure 3

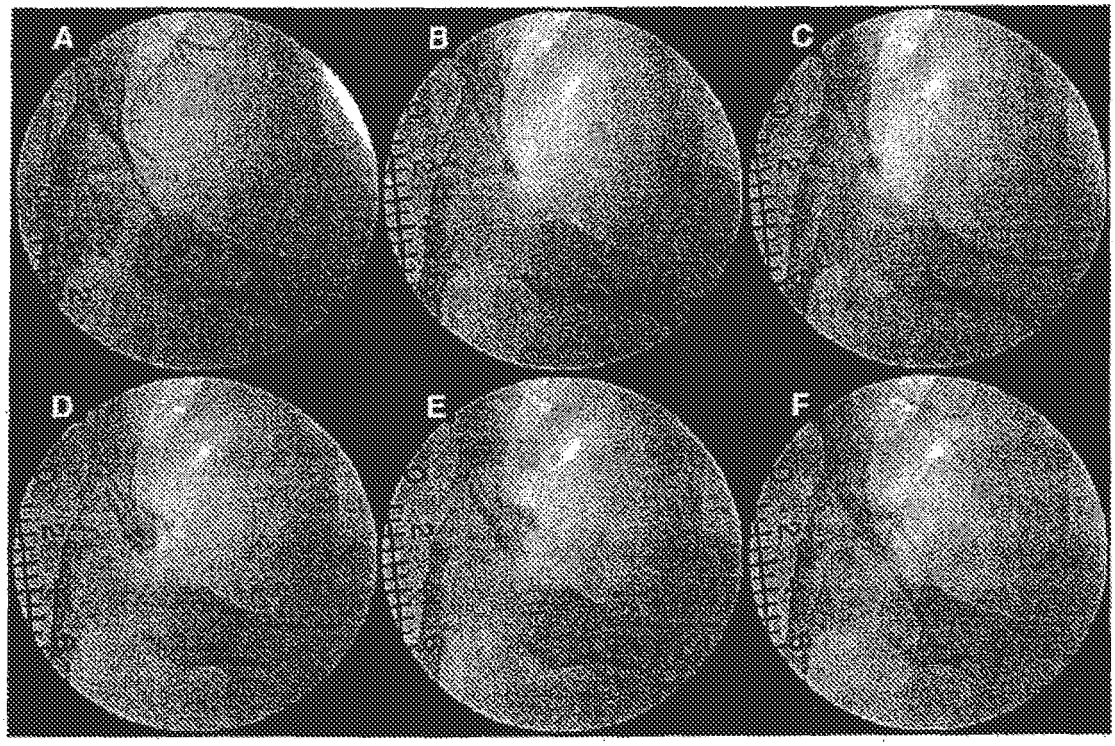


Figure 4

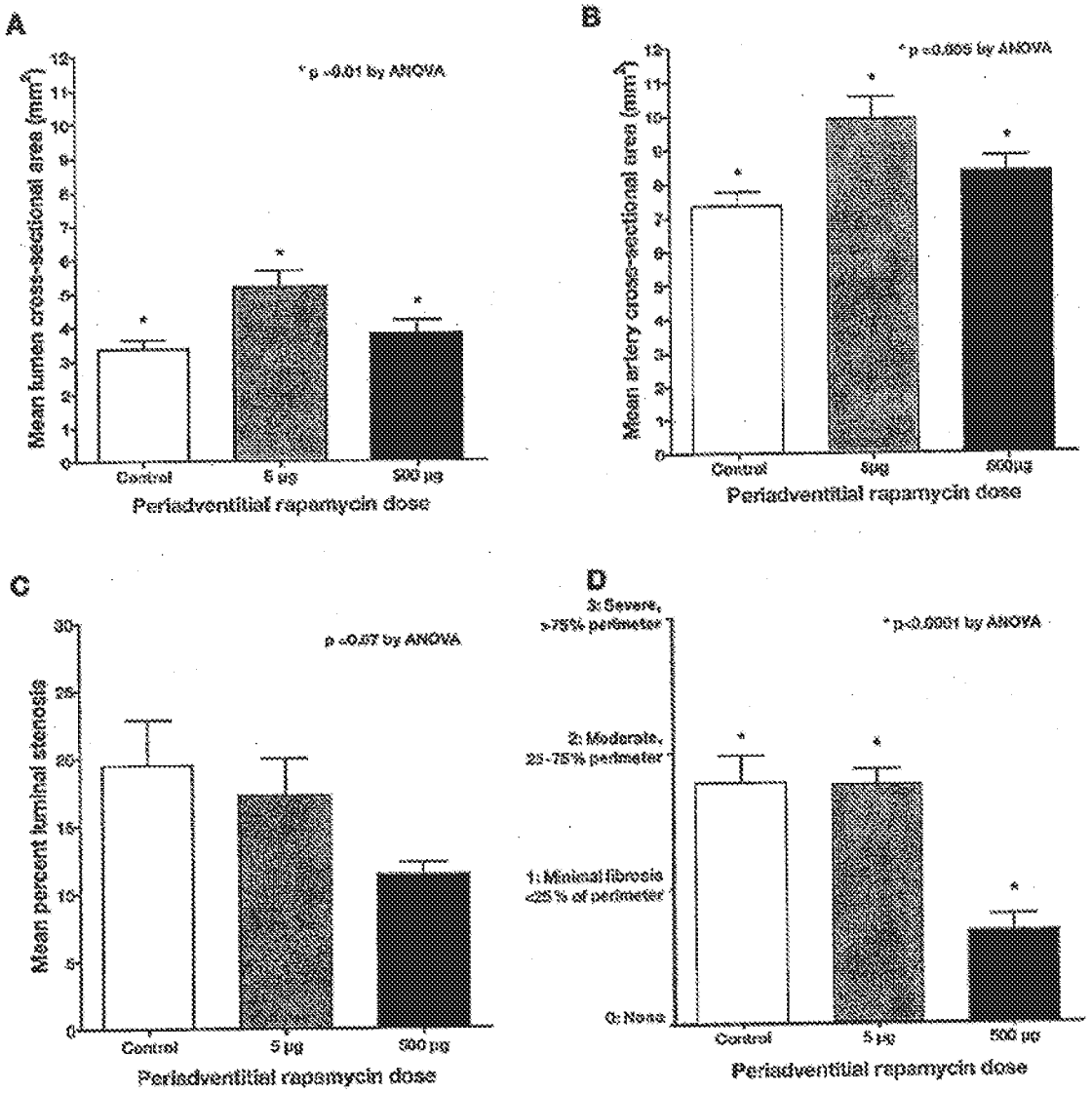

A
* p <0.01 by ANOVA
Mean lumen cross-sectional area (mm²)
Control
5 µg
500 µg
Periadventitial rapamycin dose
B
* p <0.005 by ANOVA
Mean artery cross-sectional area (mm²)
Control
5µg
500µg
Periadventitial rapamycin dose
C
p <0.07 by ANOVA
Mean percent luminal stenosis
Control
5 µg
500 µg
Periadventitial rapamycin dose
D
3: Severe, >75% perimeter
2: Moderate, 25-75% perimeter
1: Minimal fibrosis <25 % of perimeter
0: None
* p<0.0001 by ANOVA
Control
5 µg
500 µg
Periadventitial rapamycin dose

Figure 5

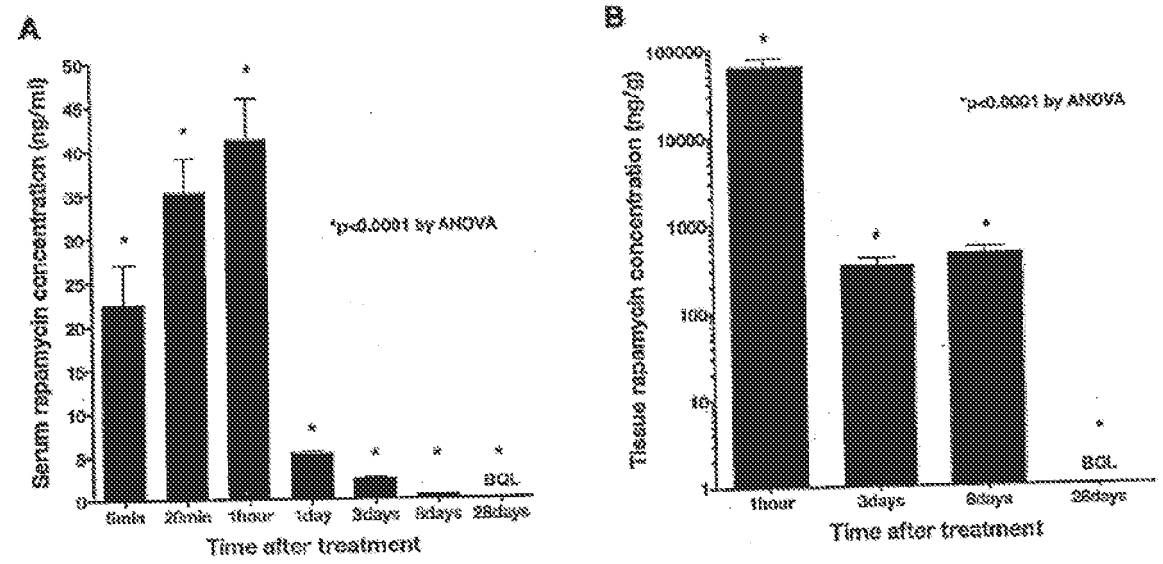

A
Serum rapamycin concentration (ng/ml)
50
45
40
35
30
25
20
15
10
5
0
*p<0.0001 by ANOVA
BQL
5min
20min
1hour
1day
3days
8days
28days
Time after treatment
B
Tissue rapamycin concentration (ng/g)
100000
10000
1000
100
10
1
*p<0.0001 by ANOVA
BQL
1hour
3days
8days
28days
Time after treatment

Figure 6

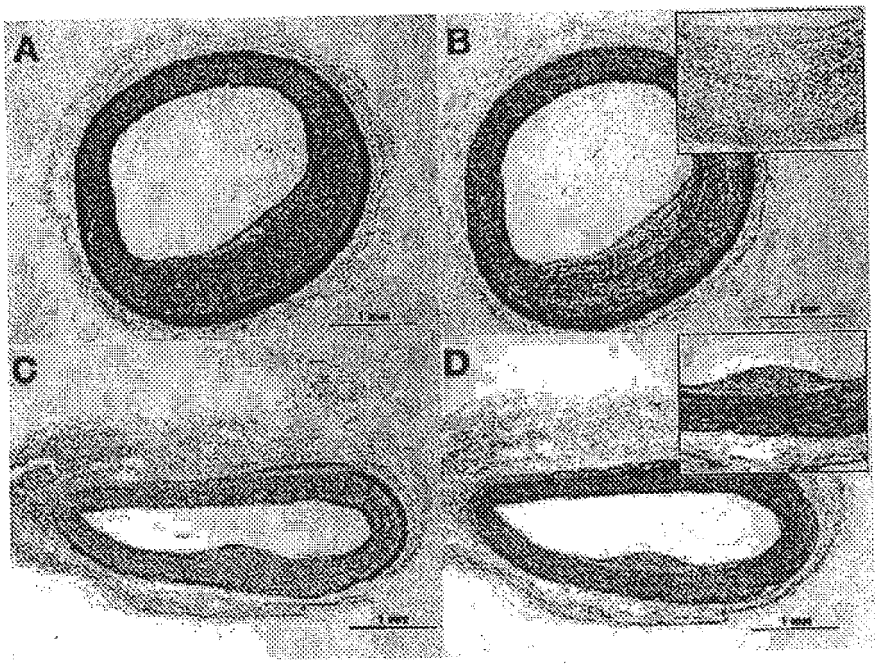


Figure 7

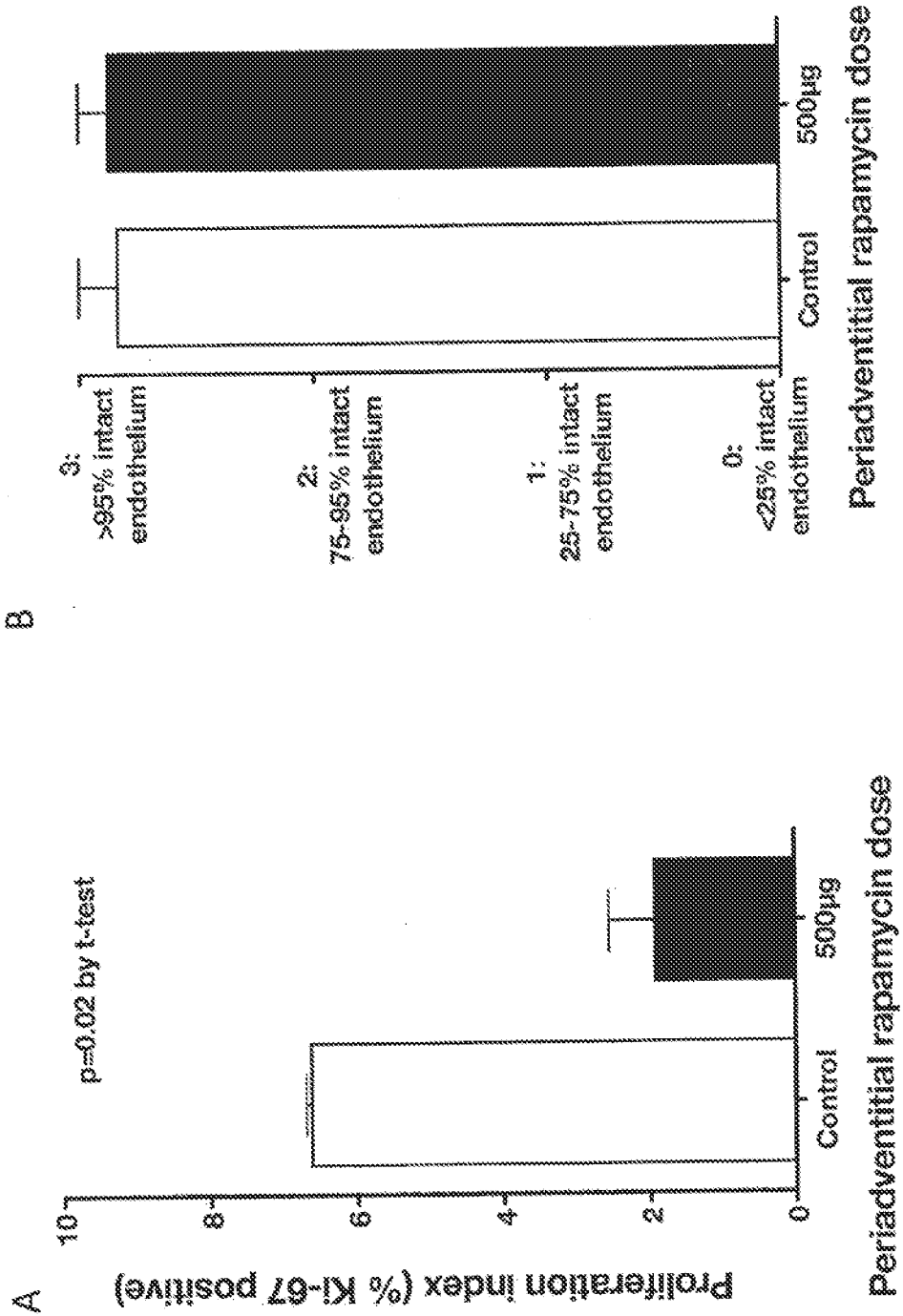

A
Proliferation index (% Ki-67 positive)
10
8
6
4
2
0
p=0.02 by t-test
Control
500µg
Periadventitial rapamycin dose
B
3:
>95% intact
endothelium
2:
75-95% intact
endothelium
1:
25-75% intact
endothelium
0:
<25% intact
endothelium
Control
500µg
Periadventitial rapamycin dose

Figure 8

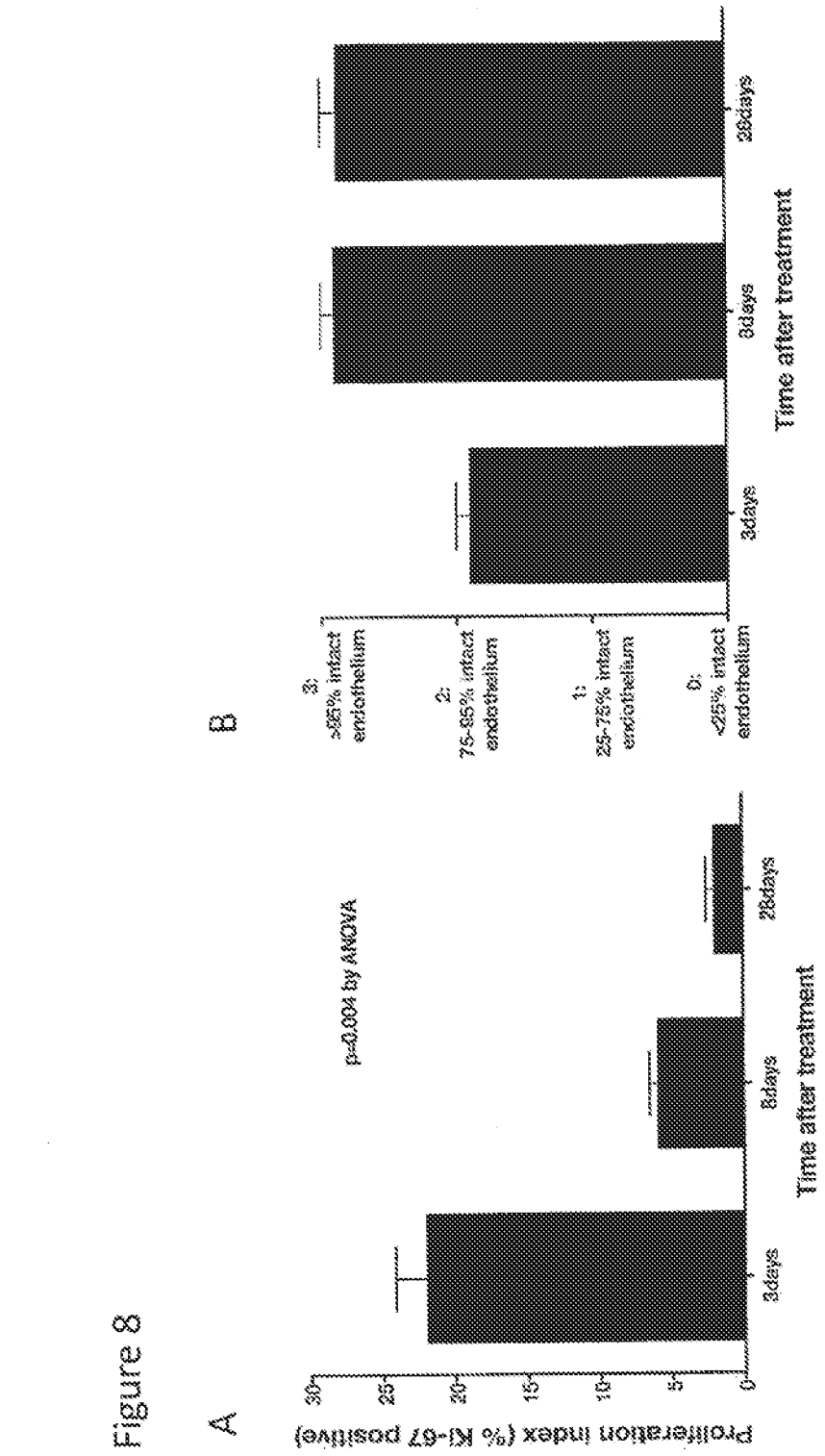
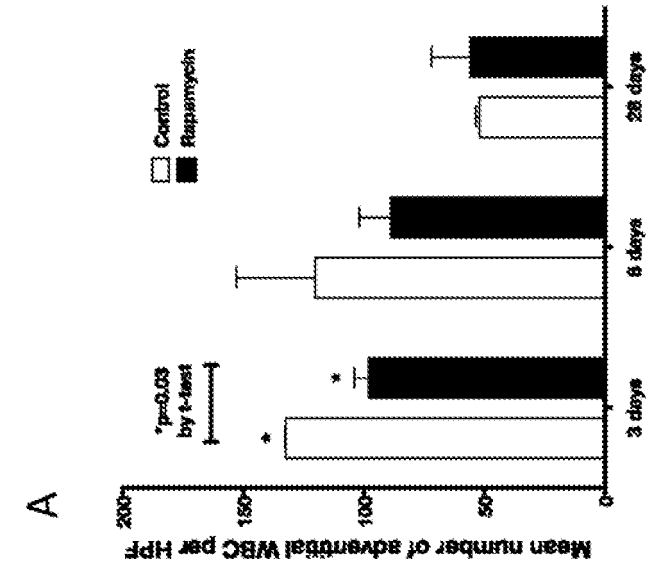

A
Proliferation index (% Ki-67 positive)
30
25
20
15
10
5
0
p=0.004 by ANOVA
3days
8days
28days
Time after treatment
B
3: >95% intact endothelium
2: 75-95% intact endothelium
1: 25-75% intact endothelium
0: <25% intact endothelium
3days
8days
28days
Time after treatment

Figure 9


A
Mean number of adventitial WBC per HPF
200
150
100
50
0
*p=0.03 by t-test
*
*
3 days
6 days
28 days
Control
Rapamycin

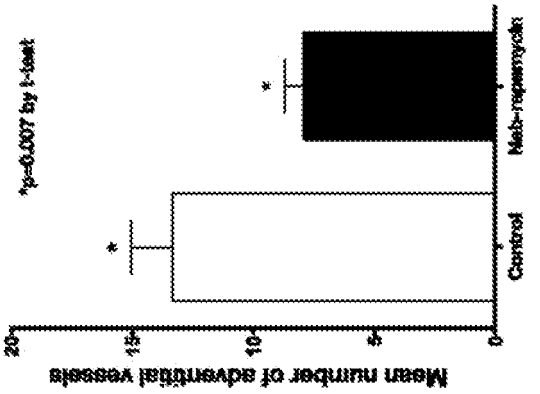
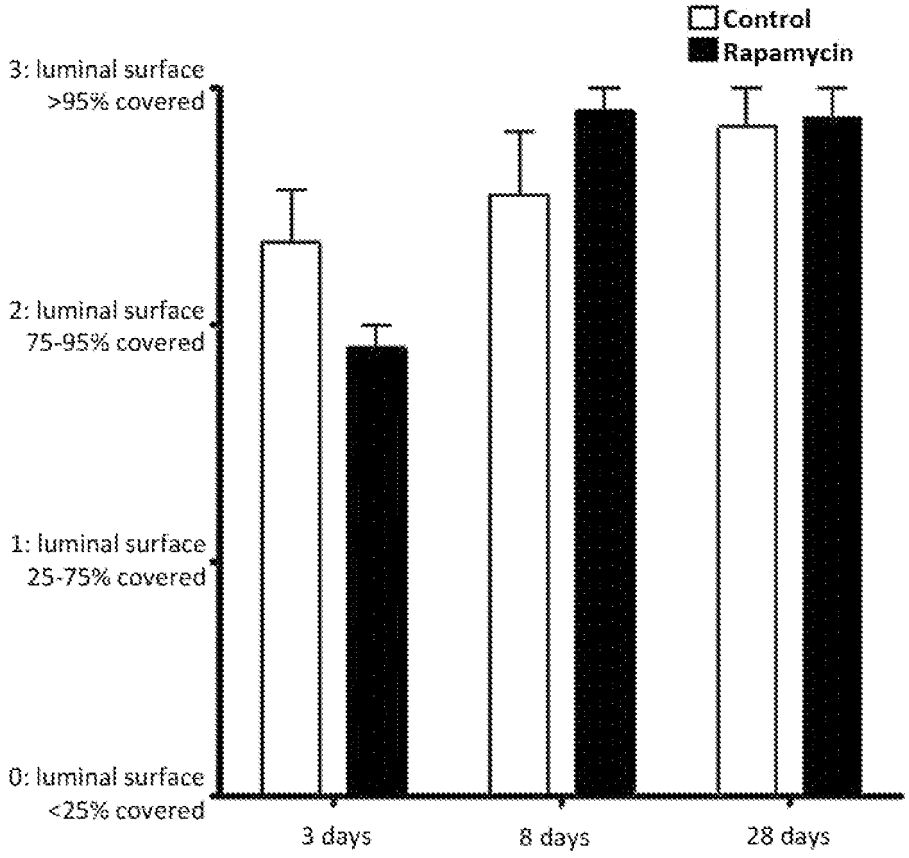

B
Mean number of adventitial vessels
20
15
10
5
0
*p=0.007 by t-test
*
*
Control
Mab-rapamycin

Figure 10


Control
Rapamycin
3: luminal surface
>95% covered
2: luminal surface
75-95% covered
1: luminal surface
25-75% covered
0: luminal surface
<25% covered
3 days
8 days
28 days