FIG. 1B

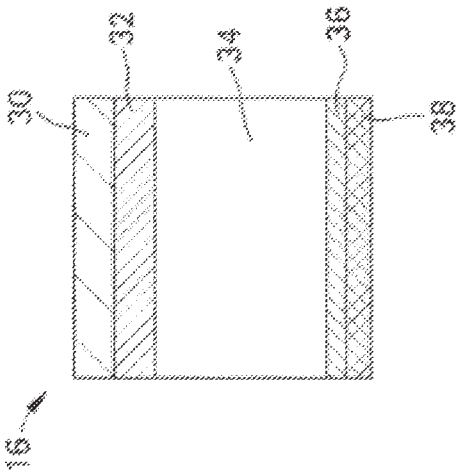


FIG. 1A

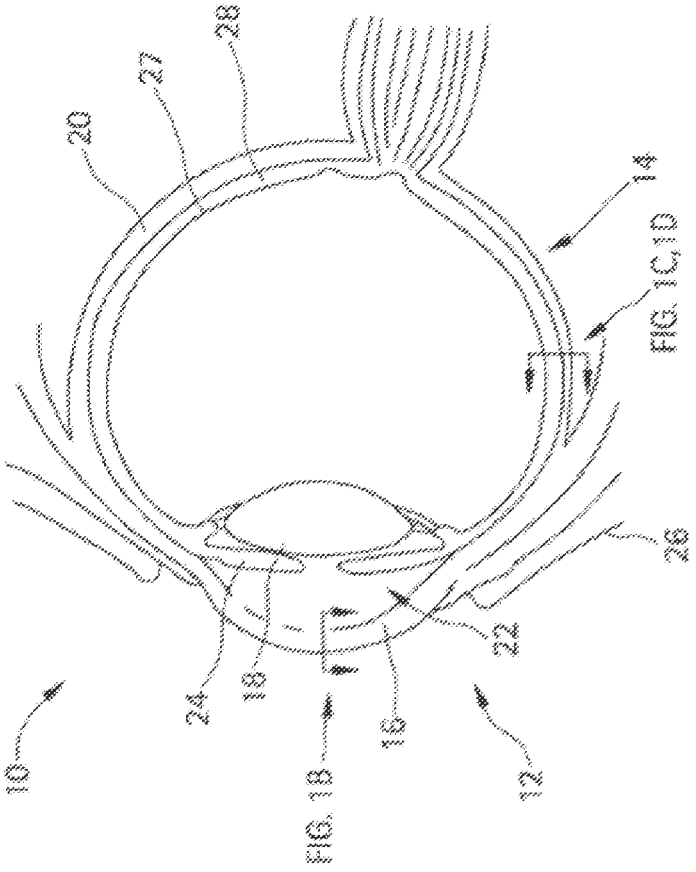


FIG. 1D

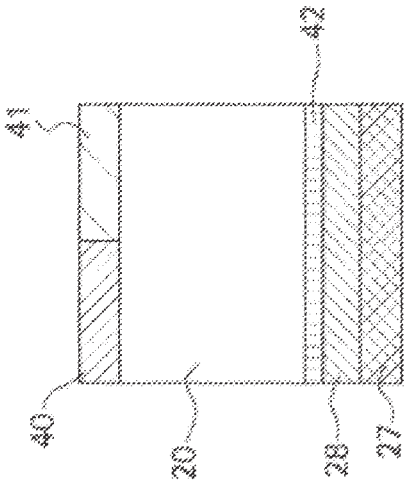


FIG. 1C

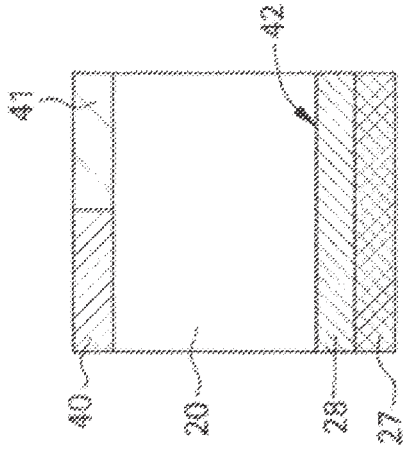


FIG. 3

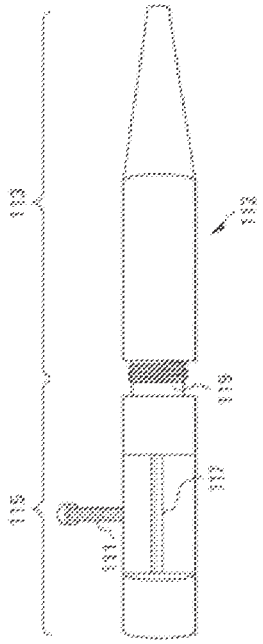


FIG. 2

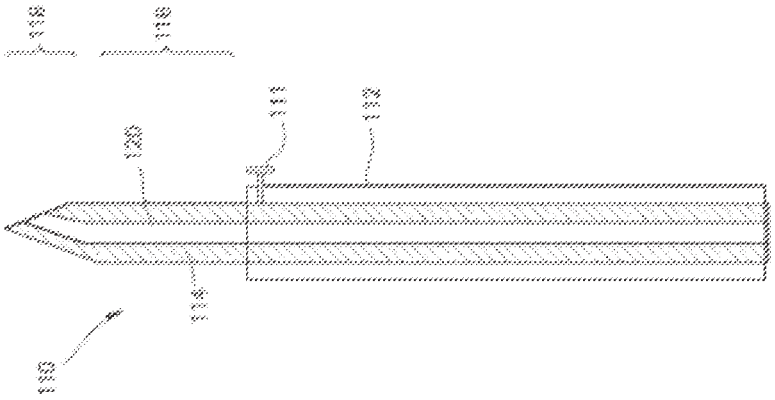


FIG. 5

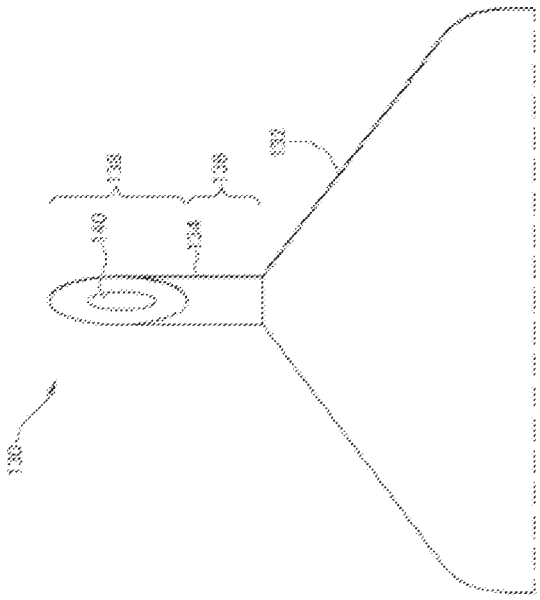


FIG. 4

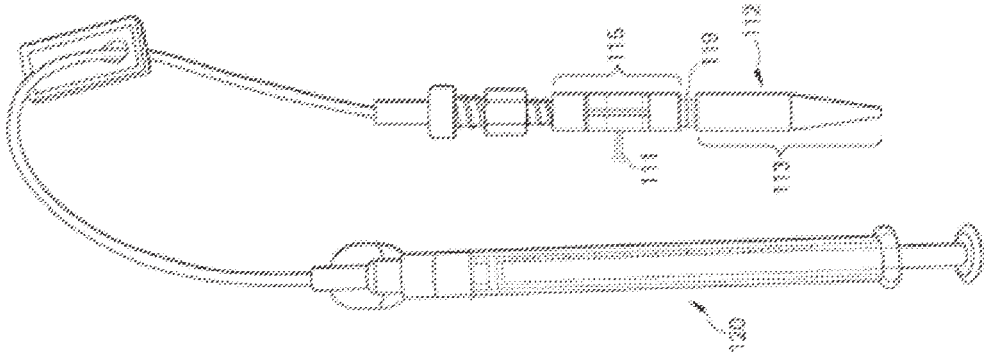


FIG. 6B

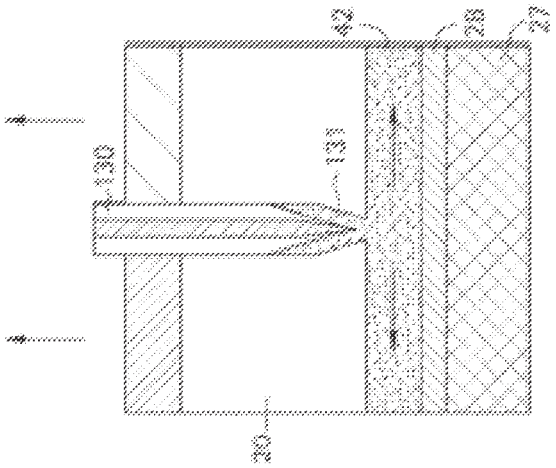


FIG. 6A

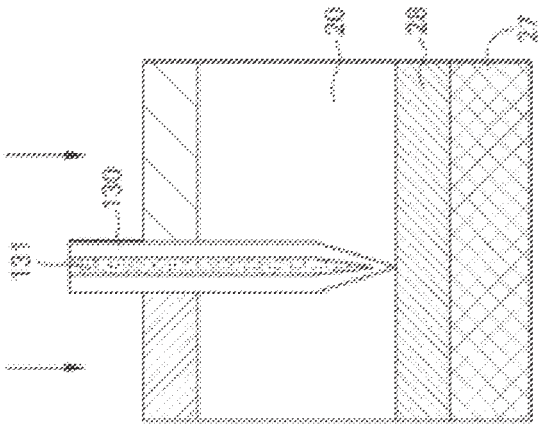


FIG. 7B

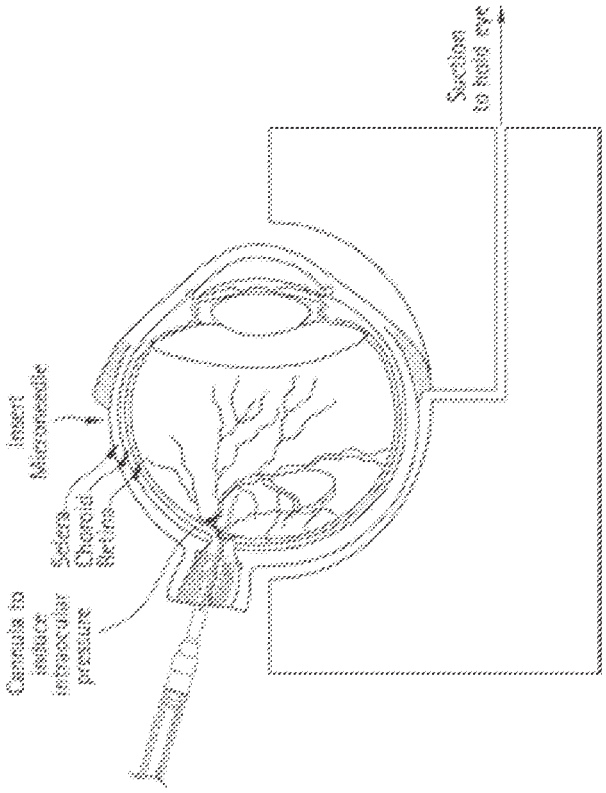

Suction to hold eye
Laser light
Cornea
Lens
Retina
Optic nerve

FIG. 7A

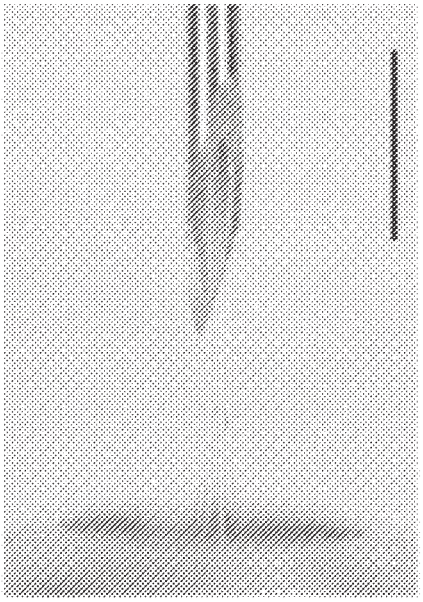


FIG. 8B

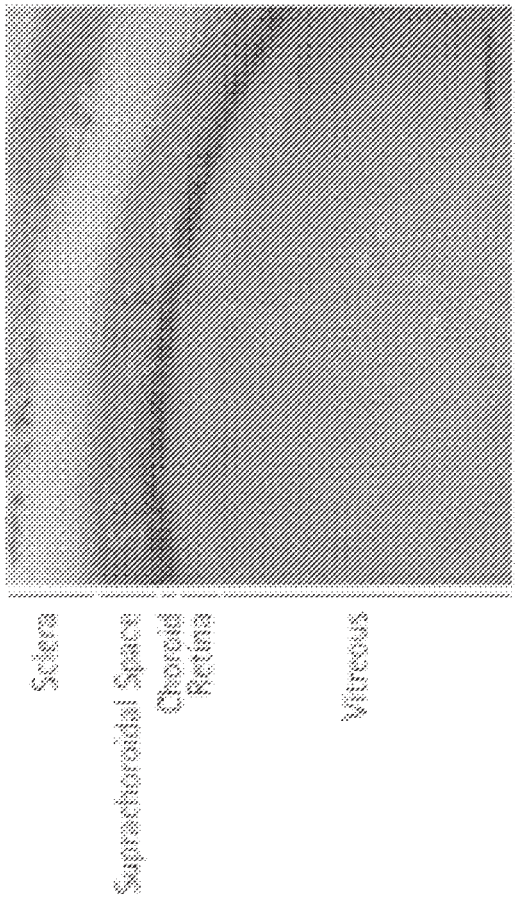

Sclera
Suprachoroidal Space
Choroid
Retina
Vitreous

FIG. 8A

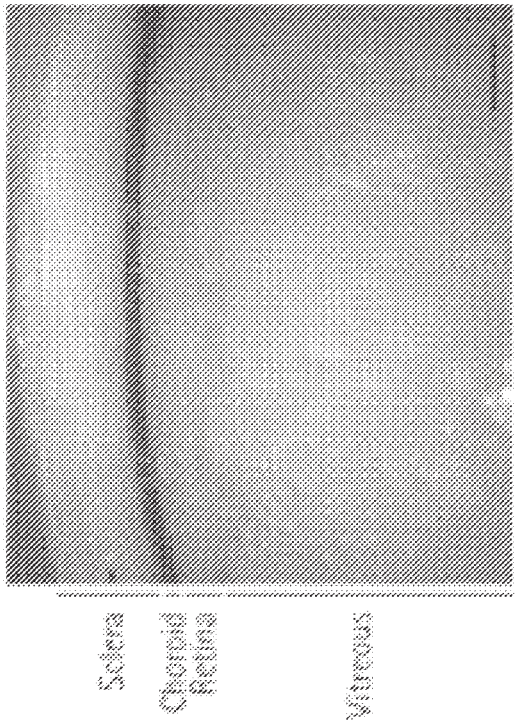

Sclera
Choroid
Retina
Vitreous

FIG. 9A

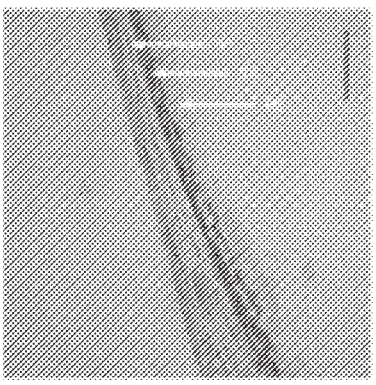


FIG. 9B

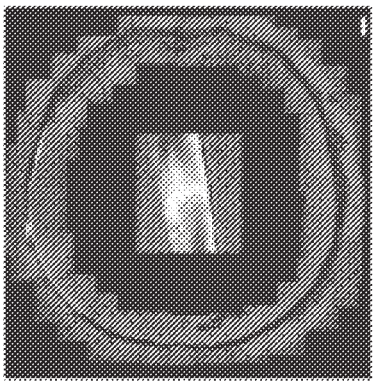


FIG. 9C

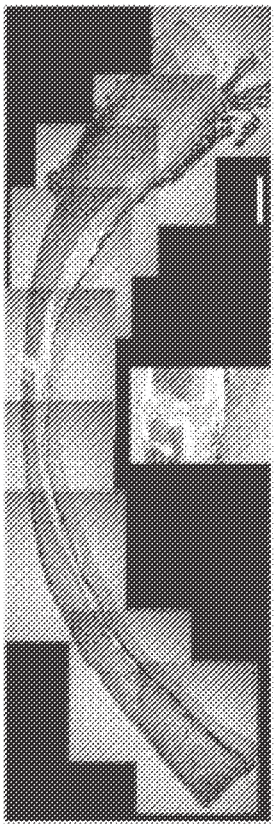


FIG. 9D

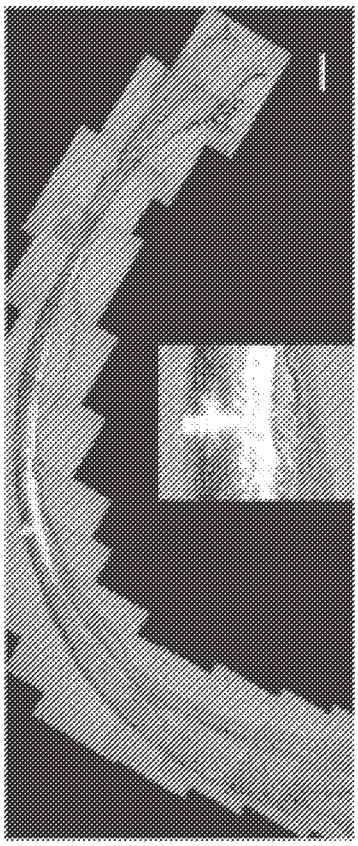


FIG. 10B

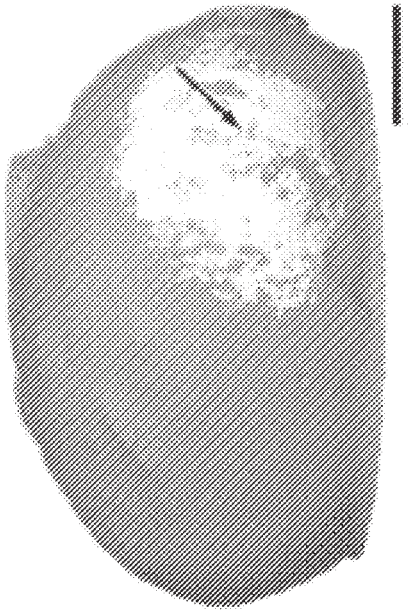


FIG. 10A

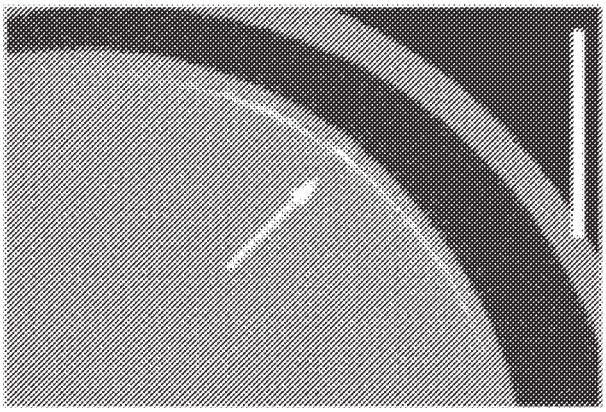


FIG. 11B

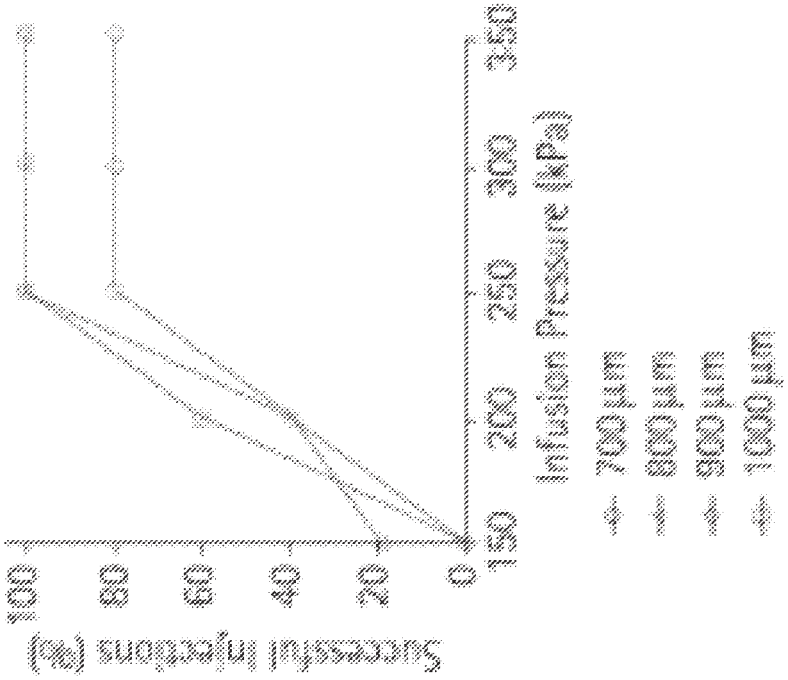


FIG. 11A

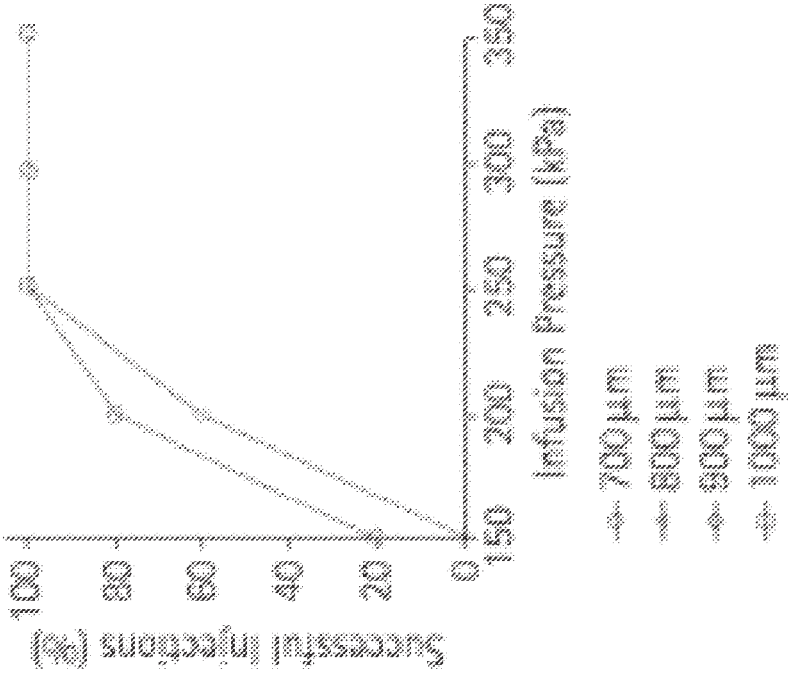


FIG. 11C

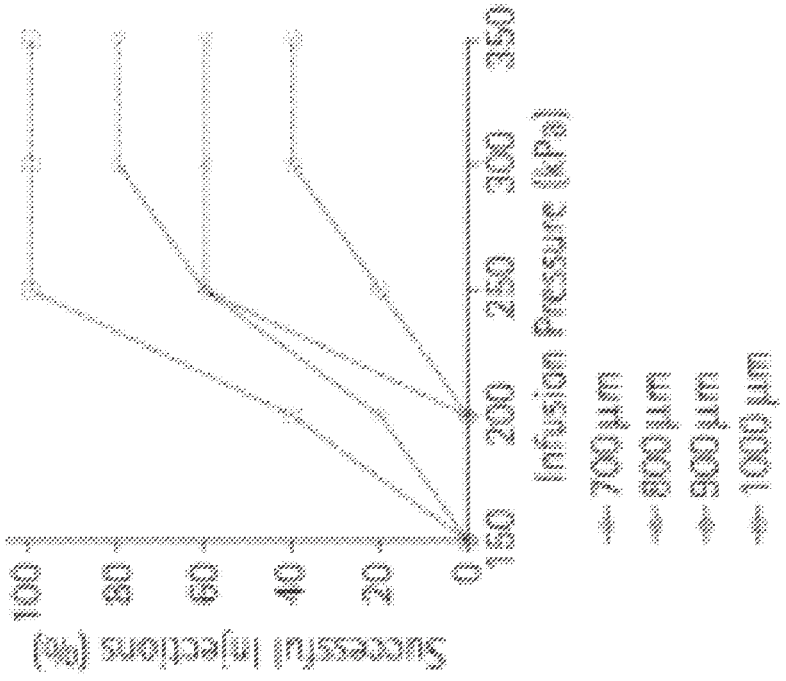


FIG. 11D

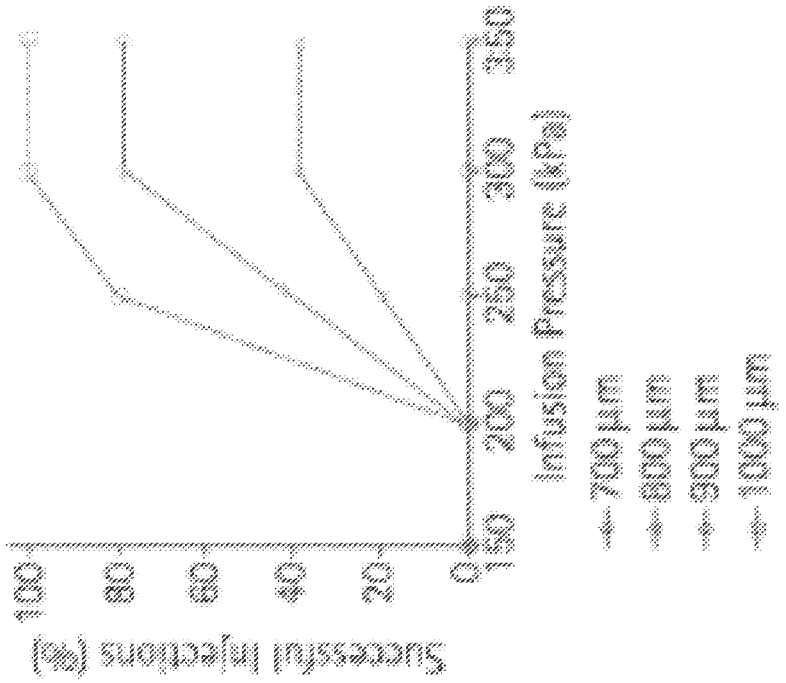


FIG. 12B

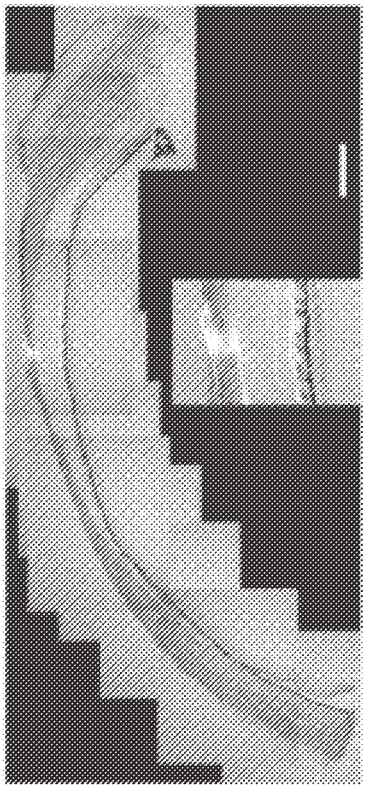


FIG. 12A



FIG. 13A

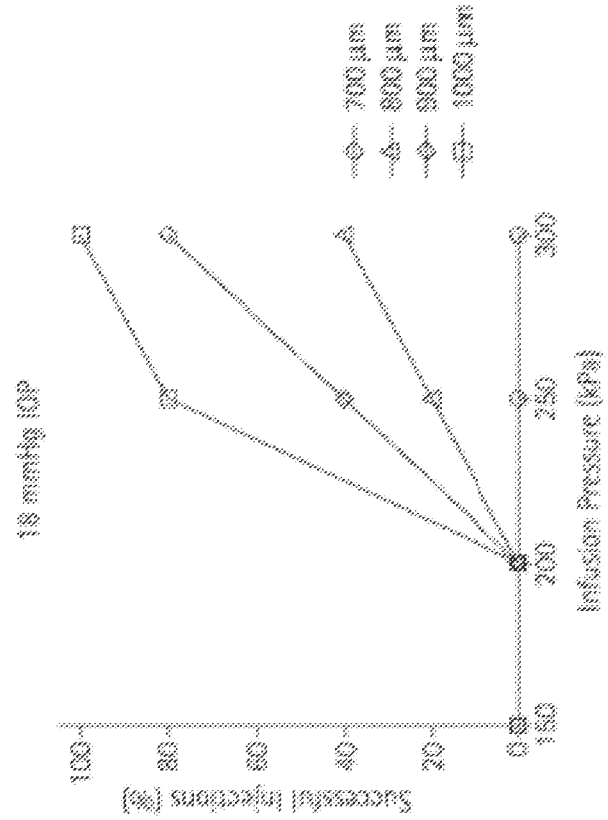


FIG. 13B

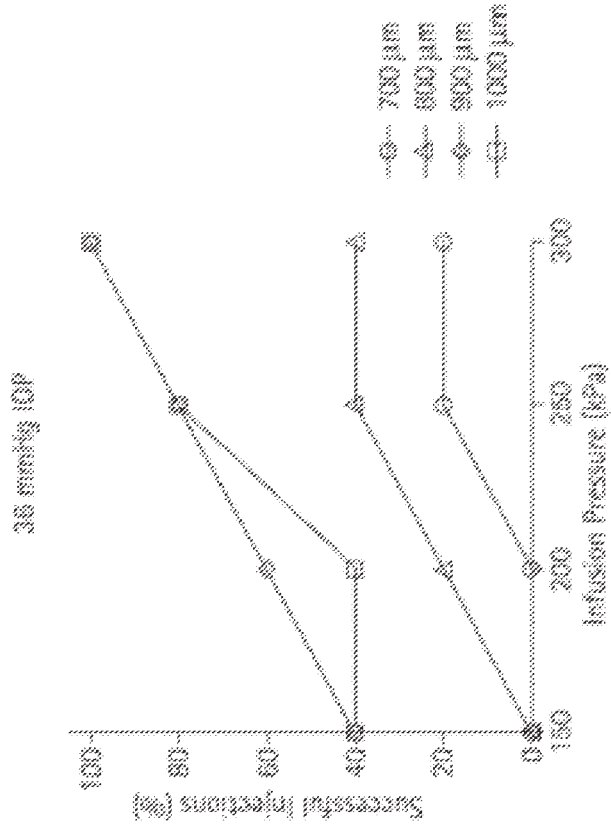


FIG. 15

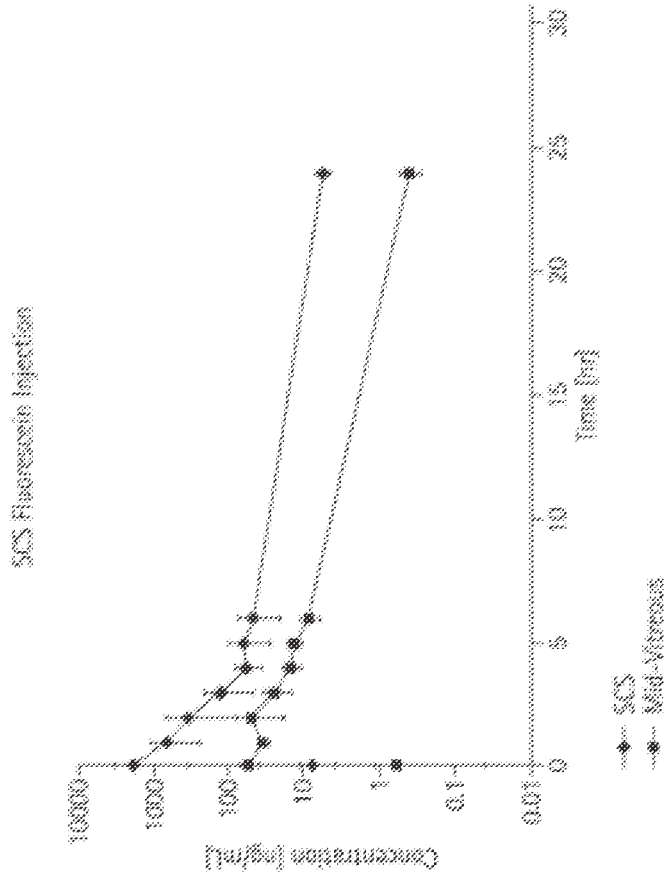

SQ fluorescein injection
Concentration [ng/mL]
1000
100
10
1
0.1
0.01
0
5
10
15
20
25
Time [hr]
SQ
Mid-Vitreous

FIG. 14

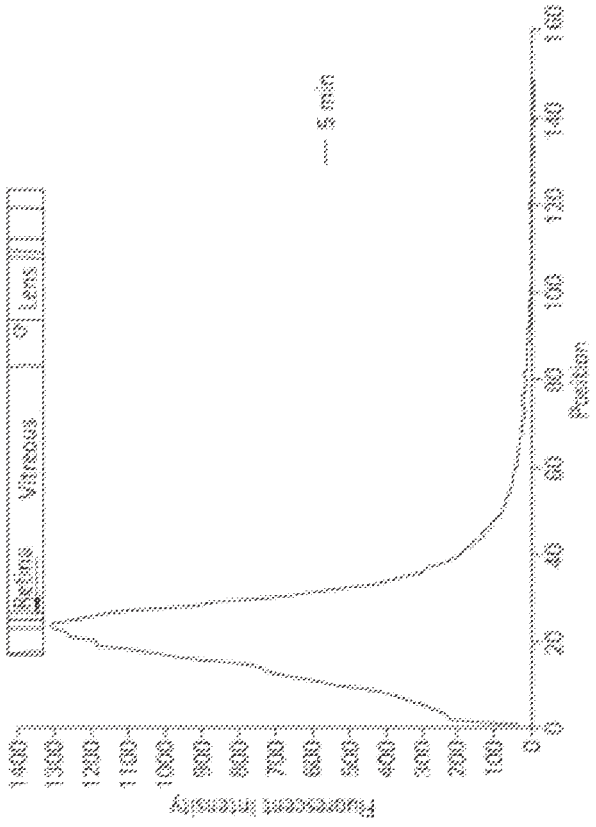

Fluorescent Intensity
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Lens
Vitreous
Retina
5 min
Position
0
20
40
60
80
100
120
140
160
180

FIG. 16

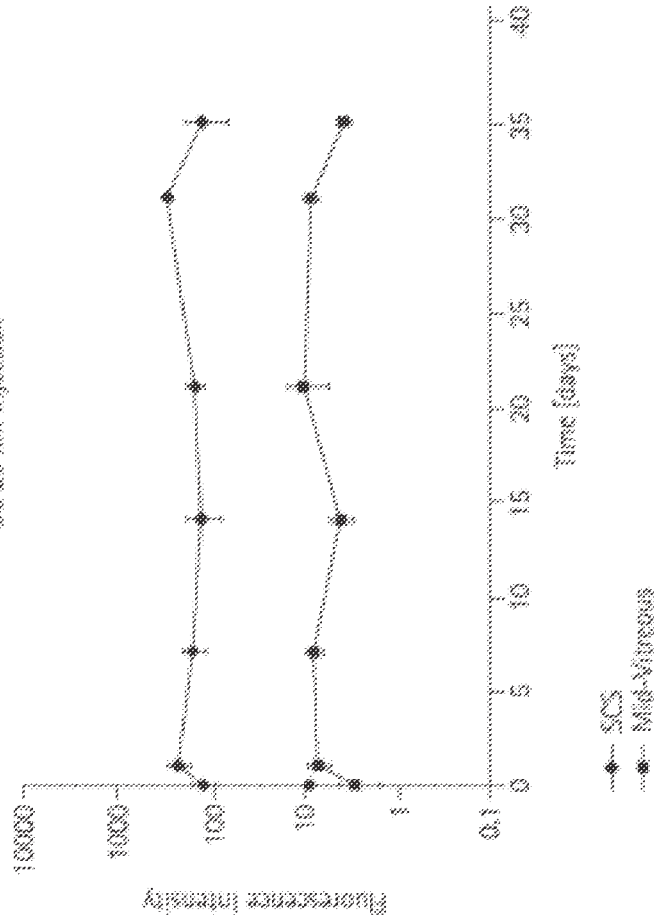

SC 40 nm Injection
Fluorescence Intensity
10000
1000
100
10
1
0.1
0
5
10
15
20
25
30
35
40
Time (days)
SC
Mid-Vitreous

FIG. 17

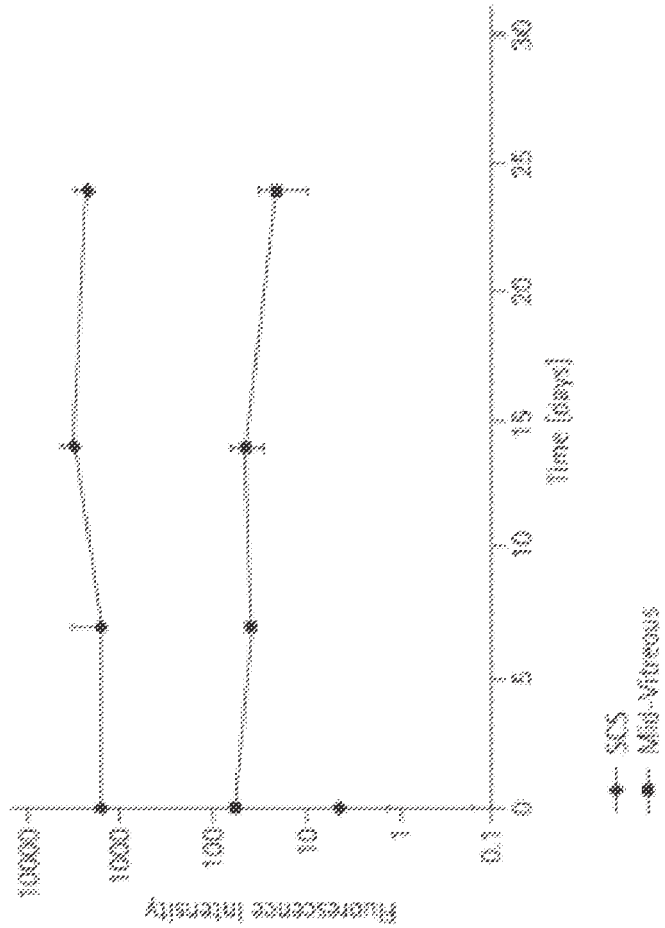

SC 500 nm Injection
Fluorescence Intensity
10000
1000
100
10
1
0.1
0
5
10
15
20
25
30
Time (days)
SC
Mid-Vitreous

FIG. 18

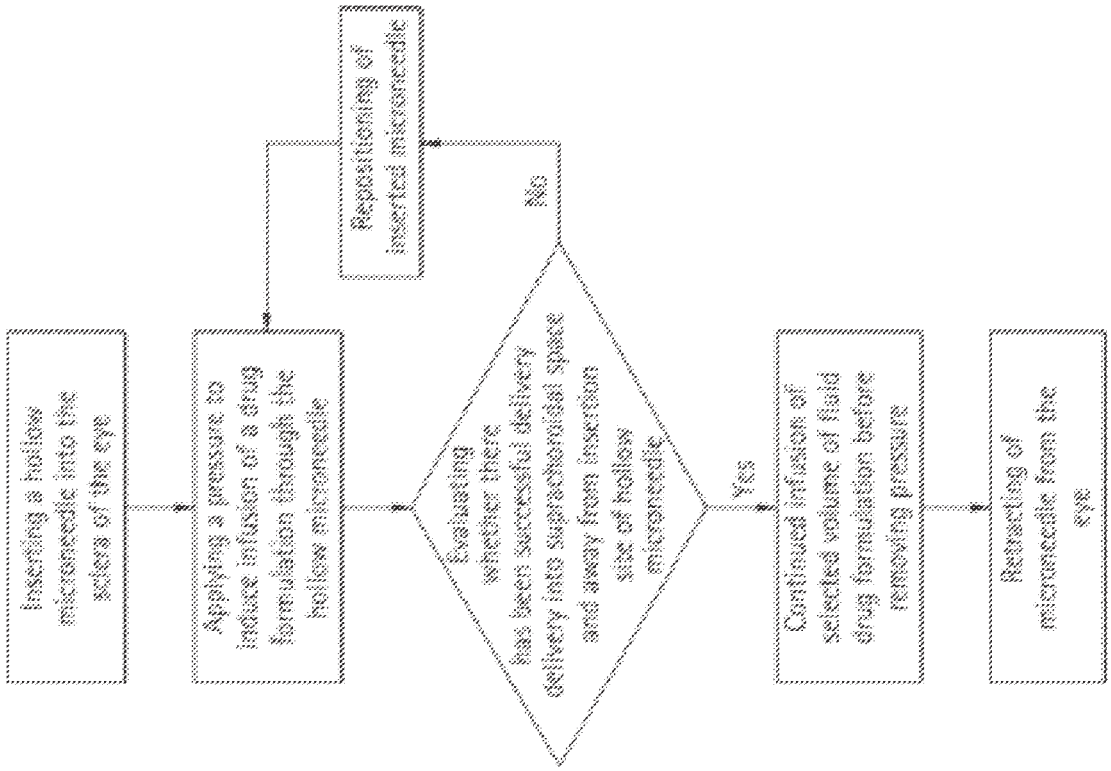

Inserting a hollow microneedle into the sclera of the eye
Applying a pressure to induce infusion of a drug formulation through the hollow microneedle
Repositioning of inserted microneedle
No
Evaluating whether there has been successful delivery into suprachoroidal space and away from insertion site of hollow microneedle
Yes
Continued infusion of selected volume of fluid drug formulation before removing pressure
Retracting of microneedle from the eye

FIG. 19A

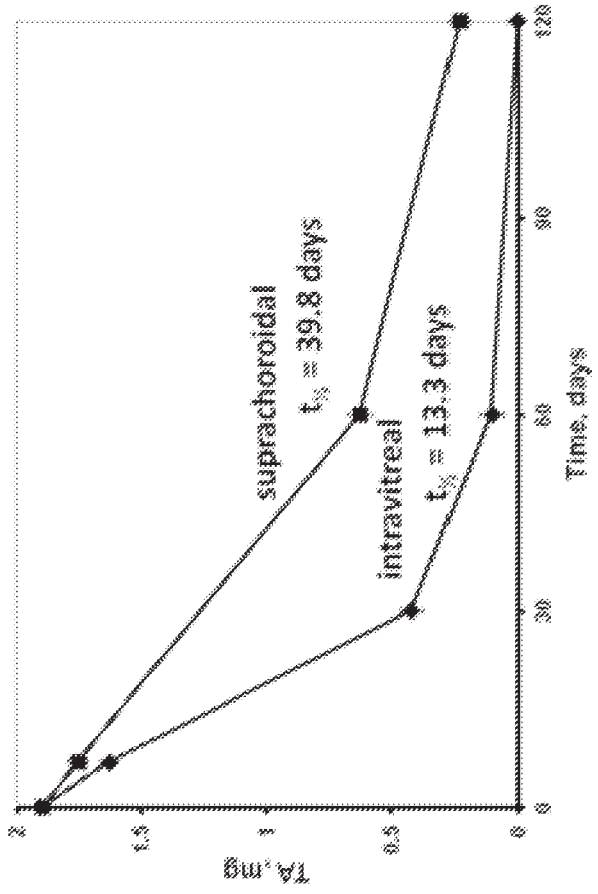


FIG. 19B

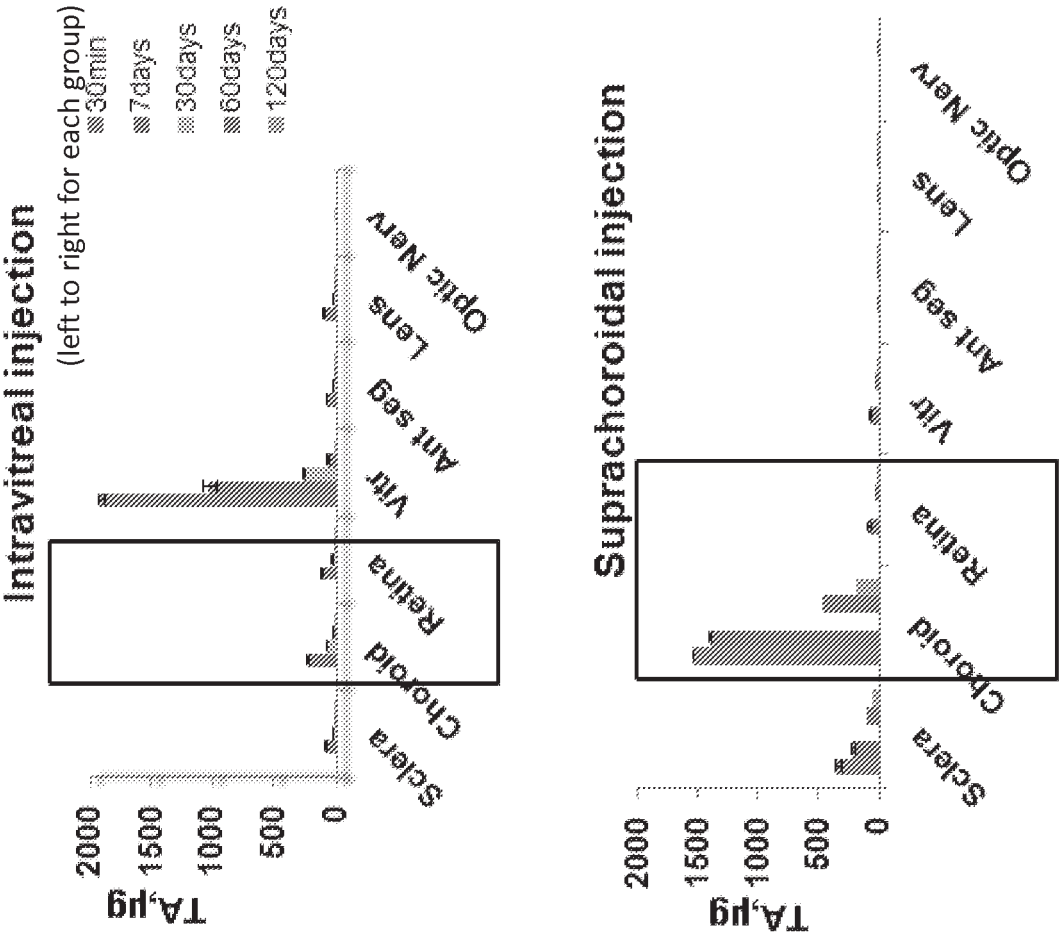


FIG. 19C

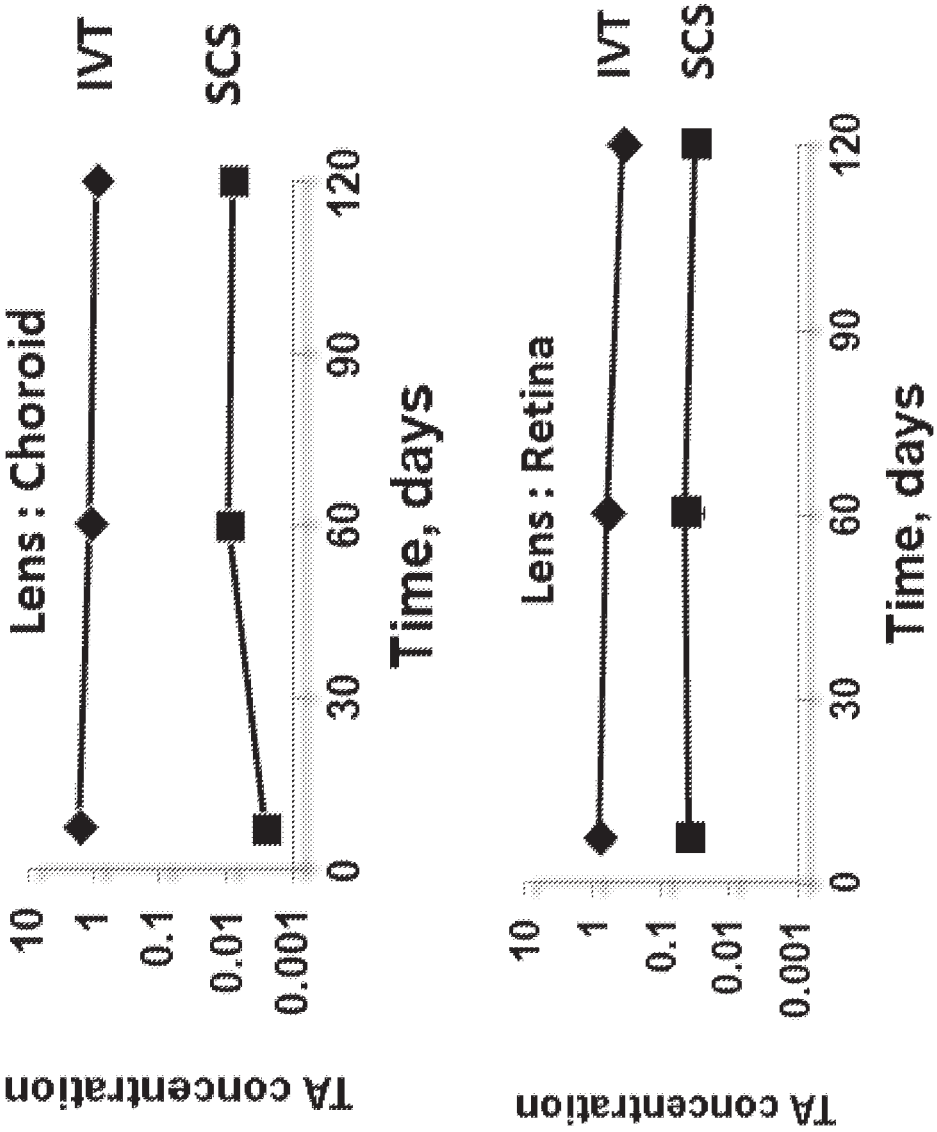
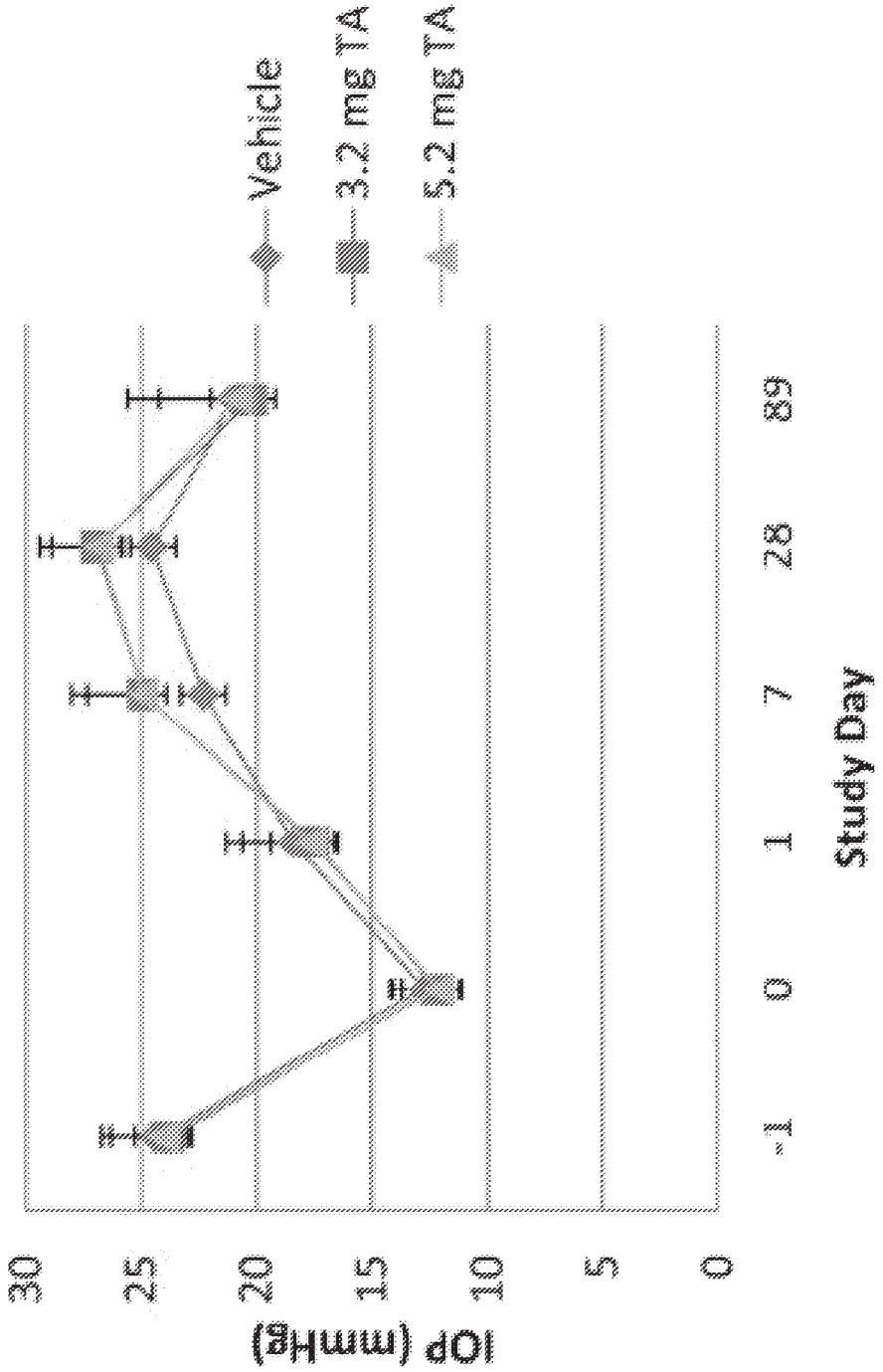

Lens : Choroid
IVT
SCS
TA concentration
10
1
0.1
0.01
0.001
0
30
60
90
120
Time, days
Lens : Retina
IVT
SCS
TA concentration
10
1
0.1
0.01
0.001
0
30
60
90
120
Time, days

FIG. 20A


Vehicle
3.2 mg TA
5.2 mg TA
IOP (mmHg)
30
25
20
15
10
5
0
-1
0
1
7
28
89
Study Day

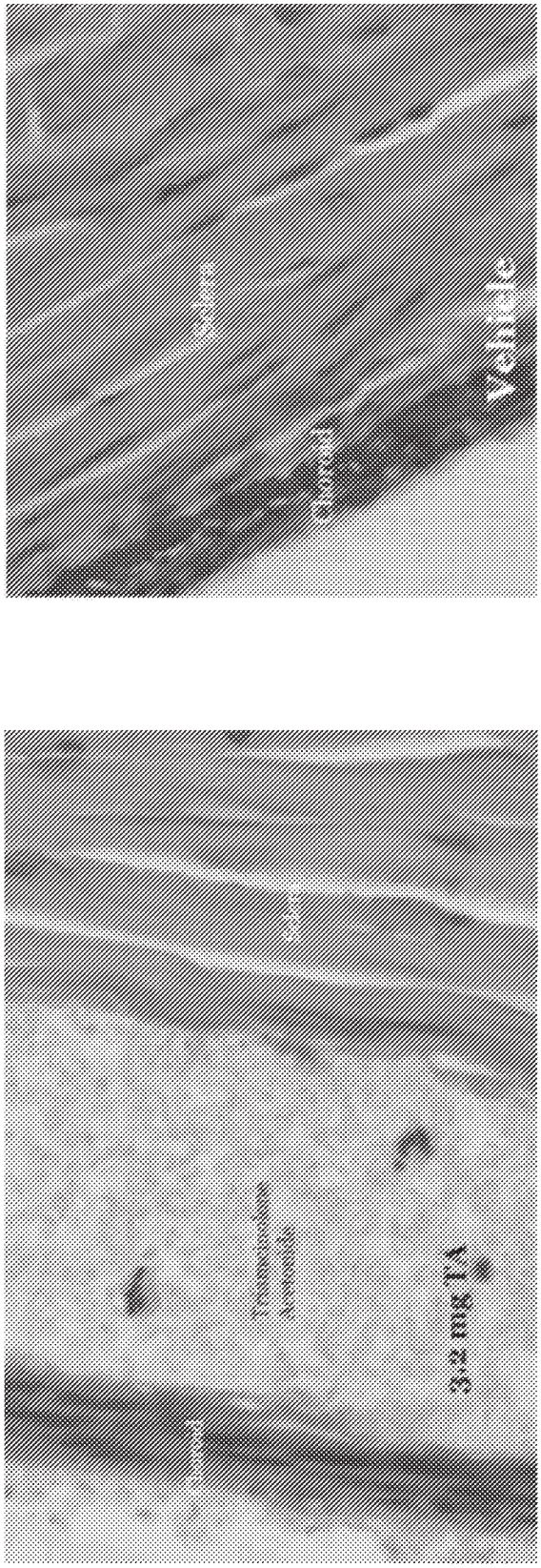
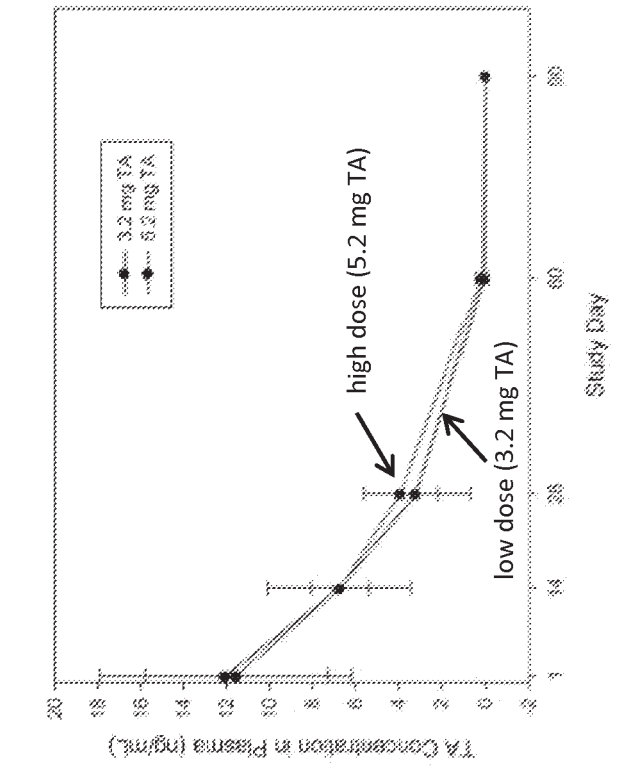


FIG. 20B

FIG. 20C

Single Dose GLP Toxicology in Rabbits
Systemic Exposure, n=10 rabbits



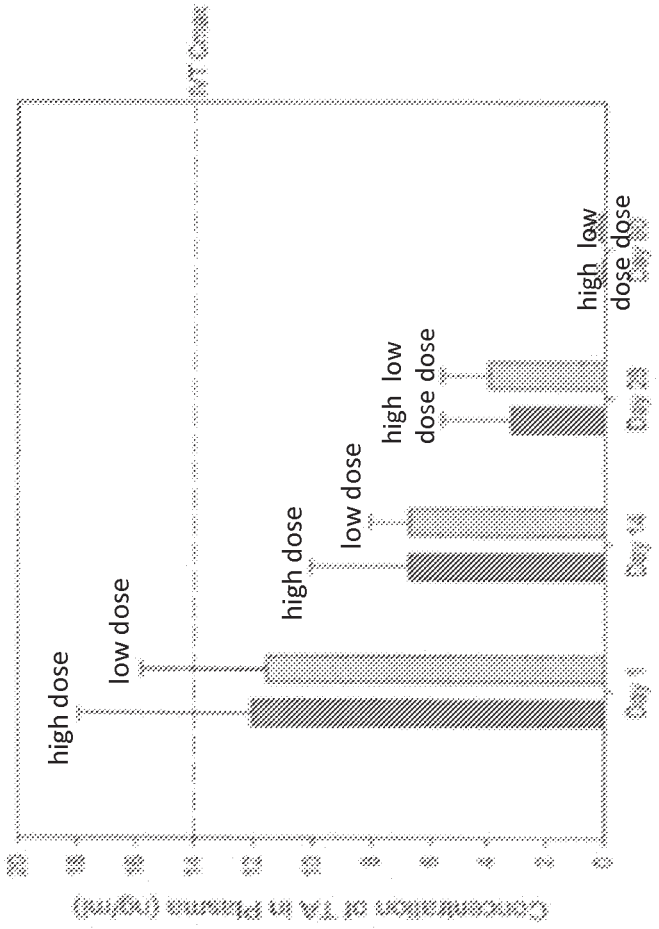


FIG. 20D

Rabbit Ocular Tissue Levels After SCS Injection of TA

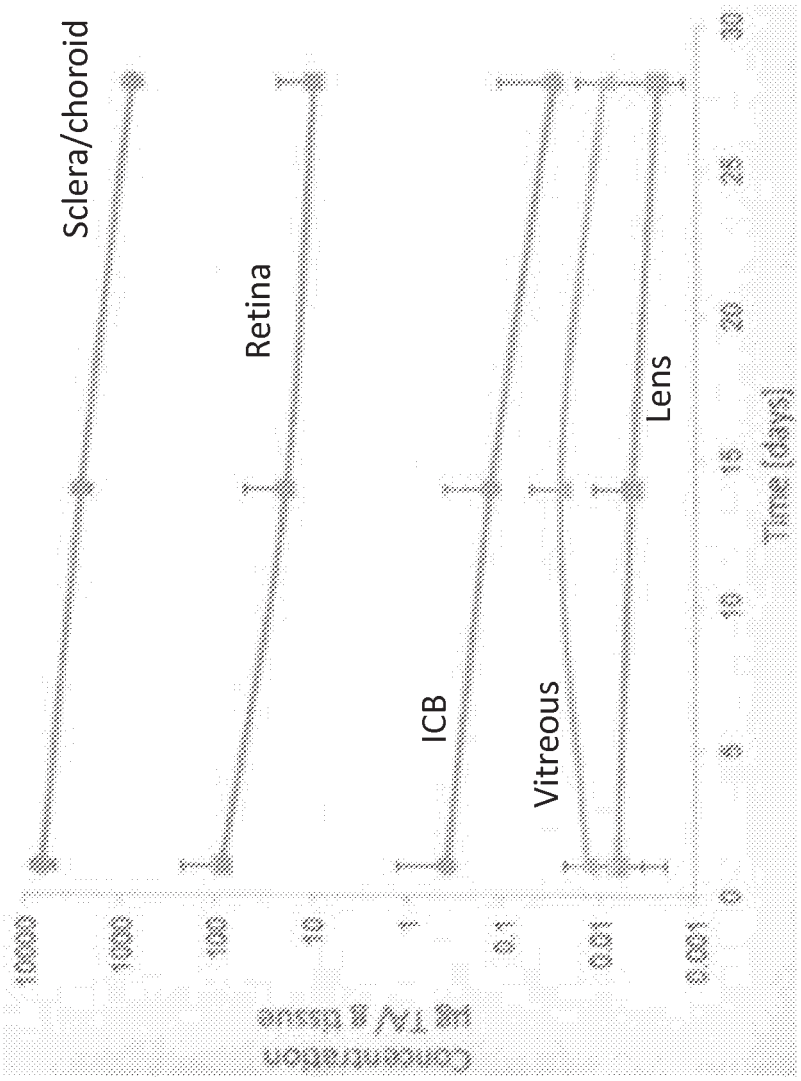


FIG. 20E

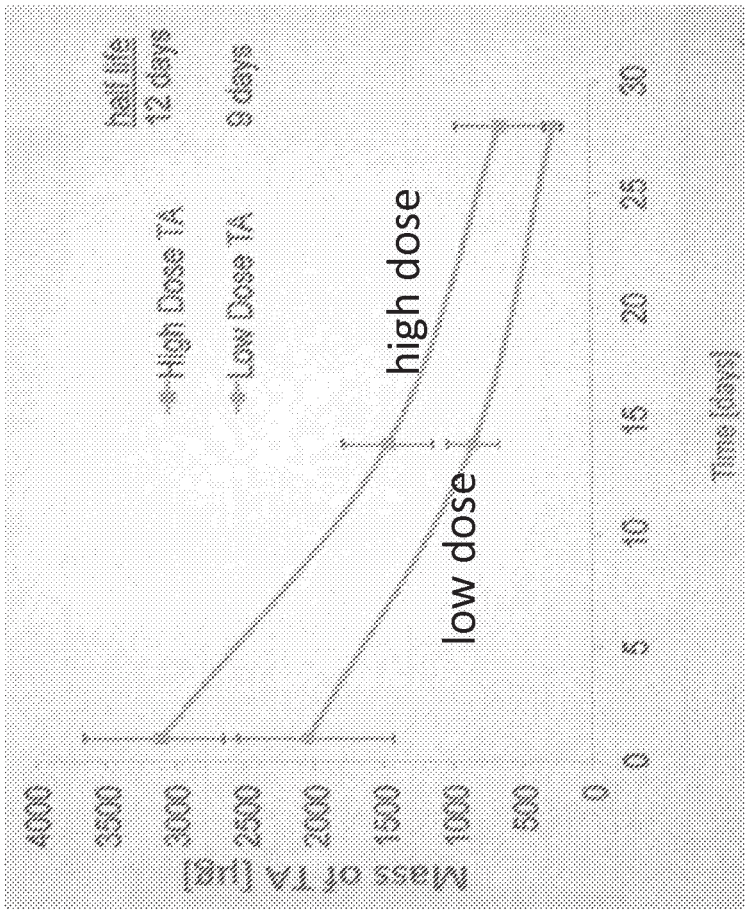


FIG. 20F

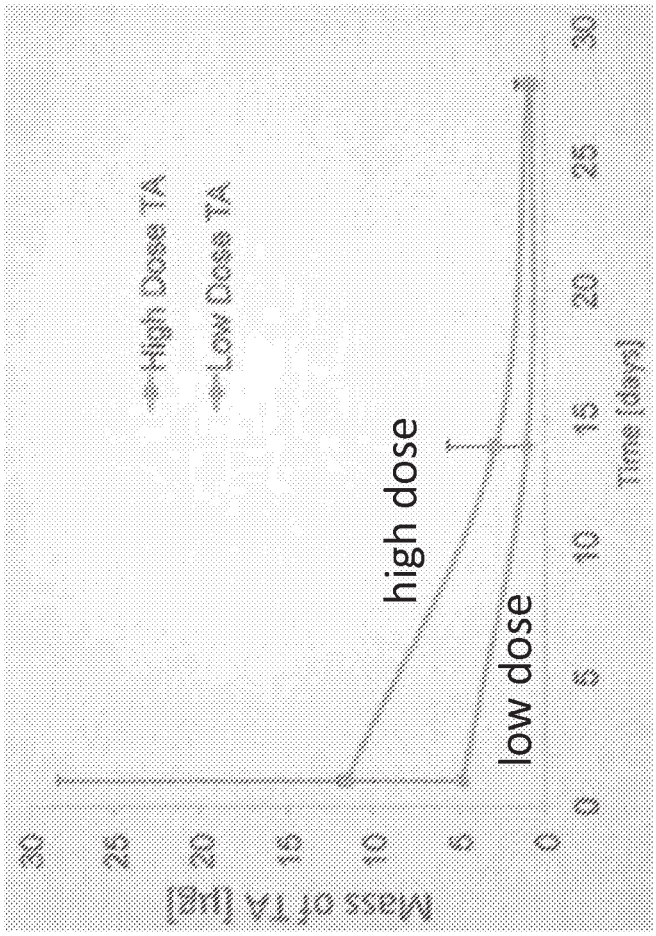


FIG. 21A

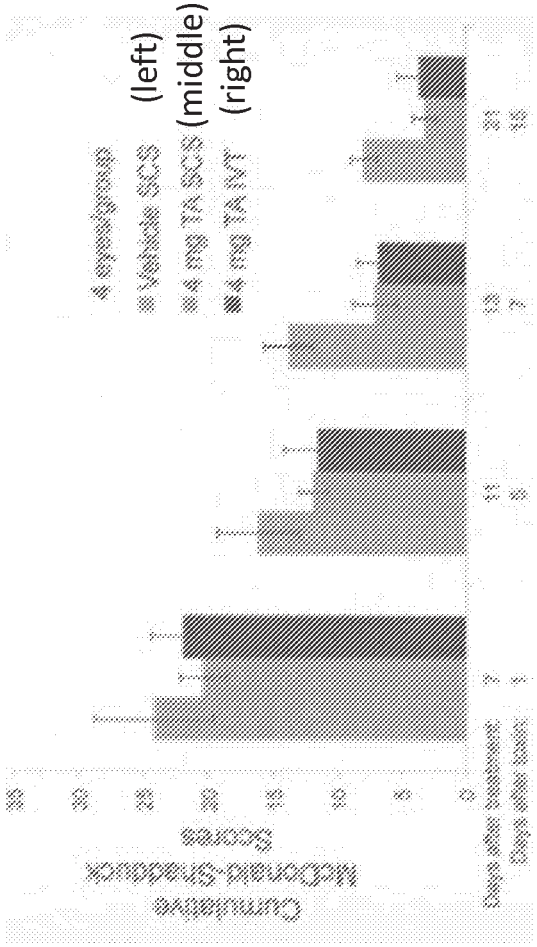


FIG. 21B

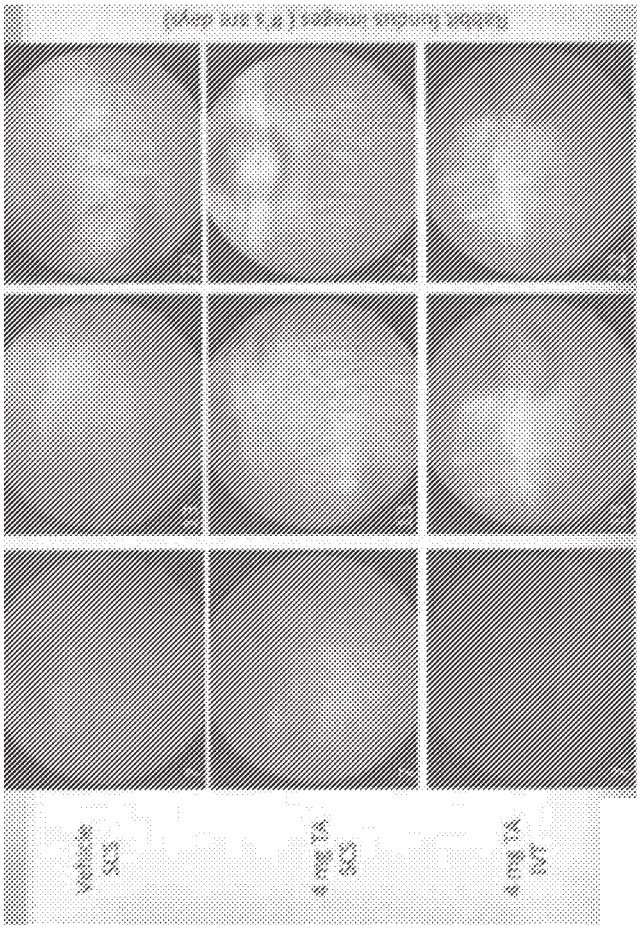


FIG. 21C

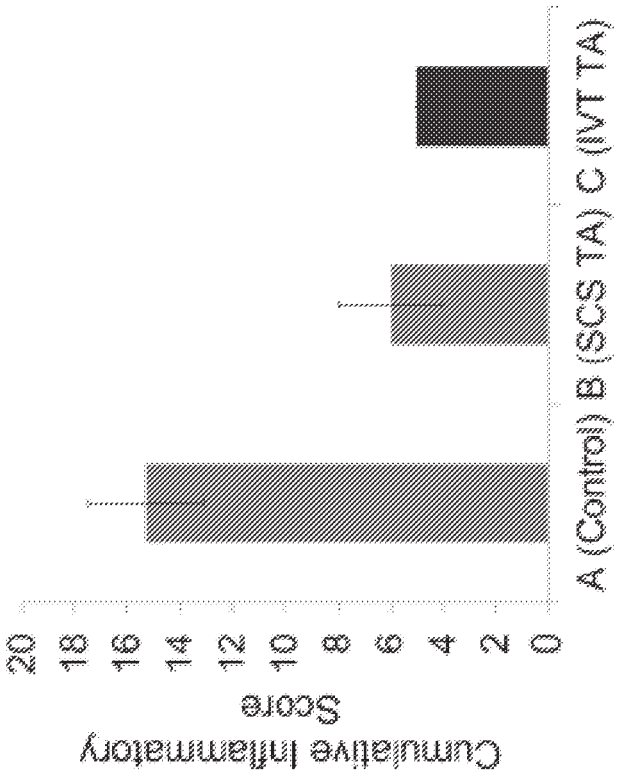


FIG. 21D

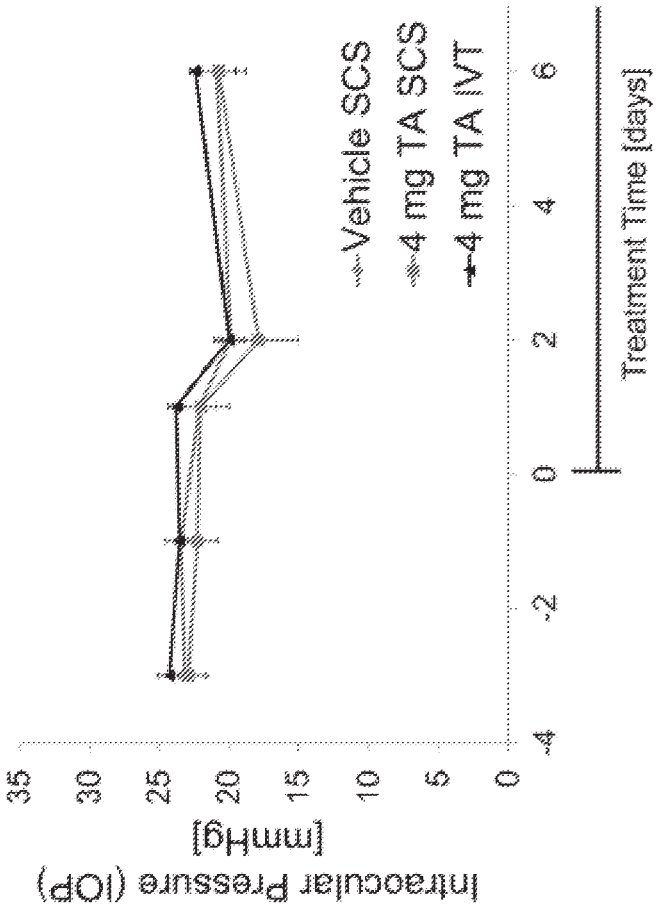


FIG. 22A

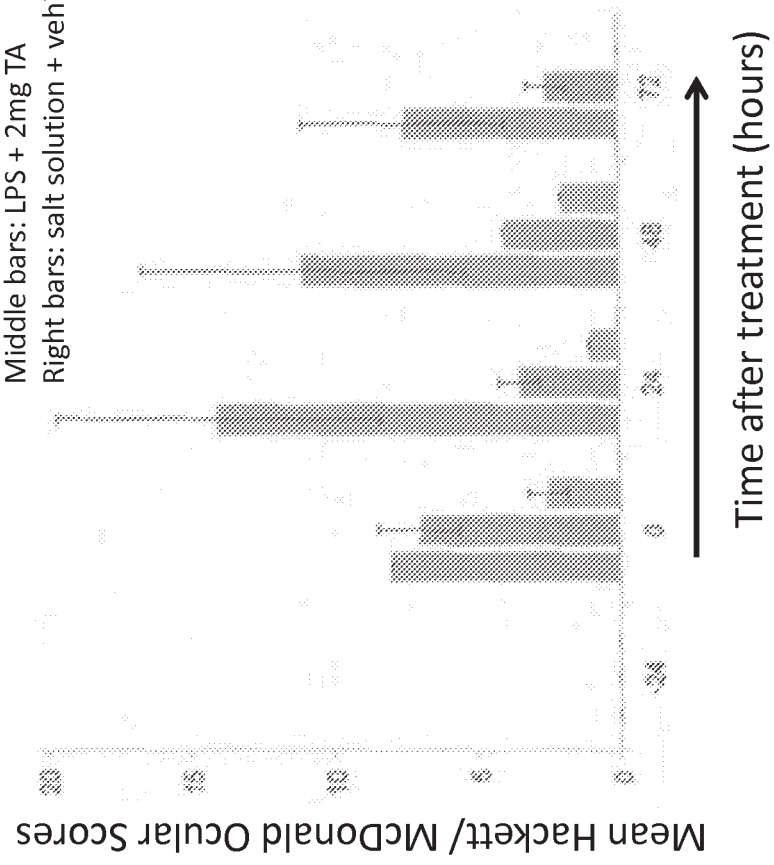


FIG. 22B

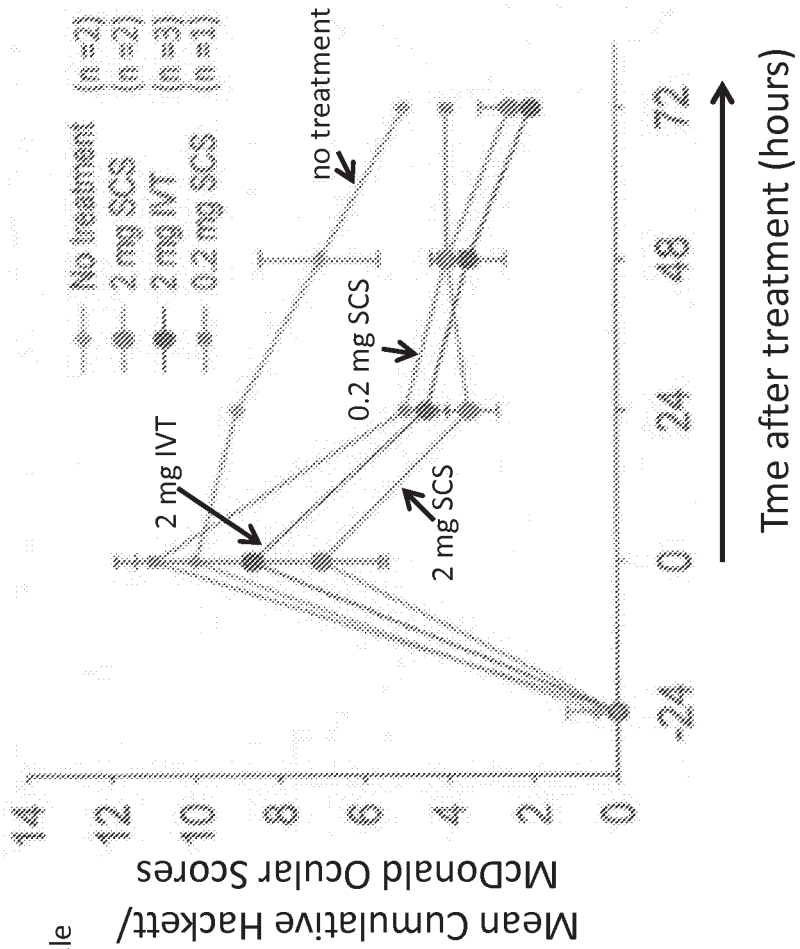


FIG. 23

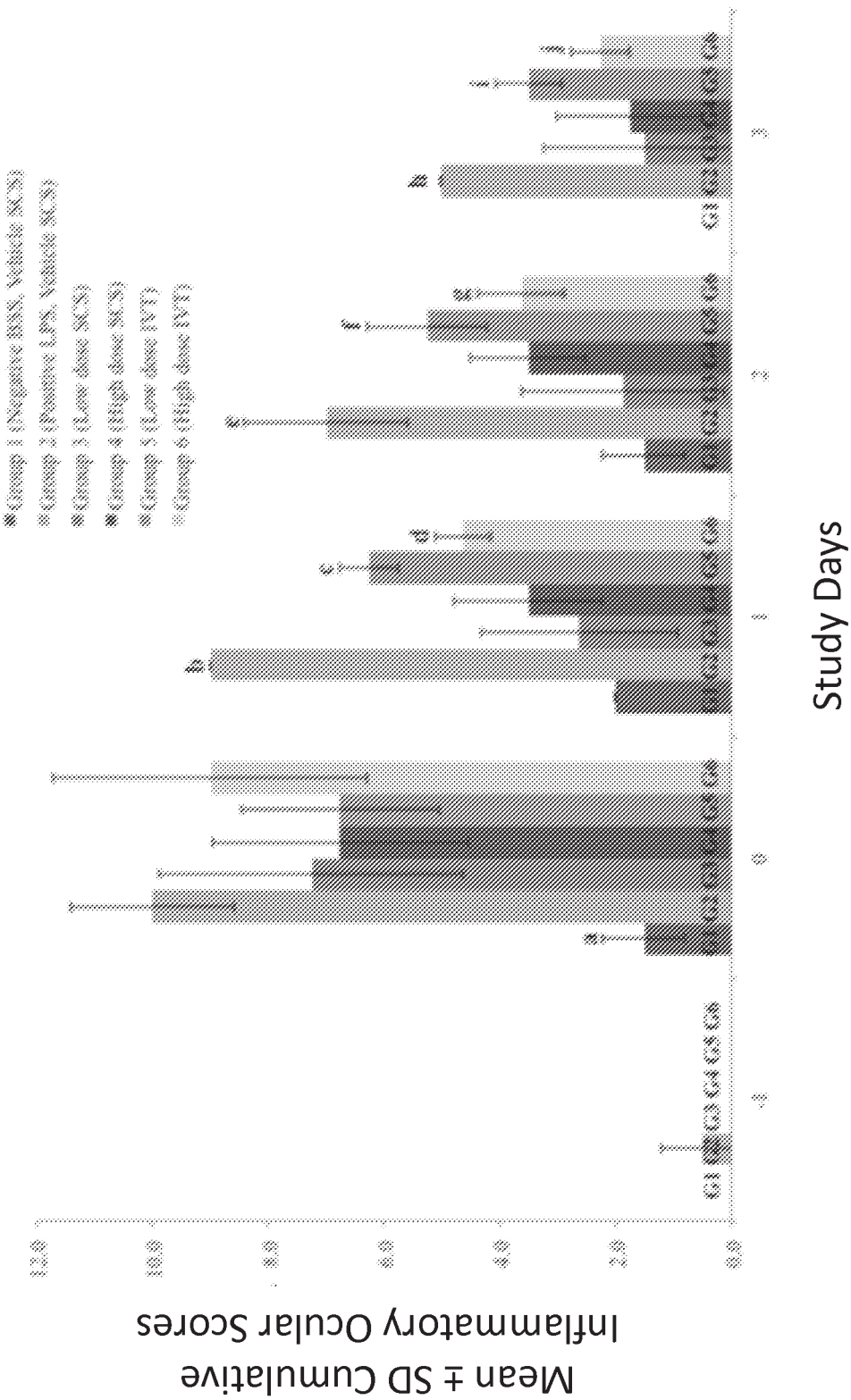


FIG. 24

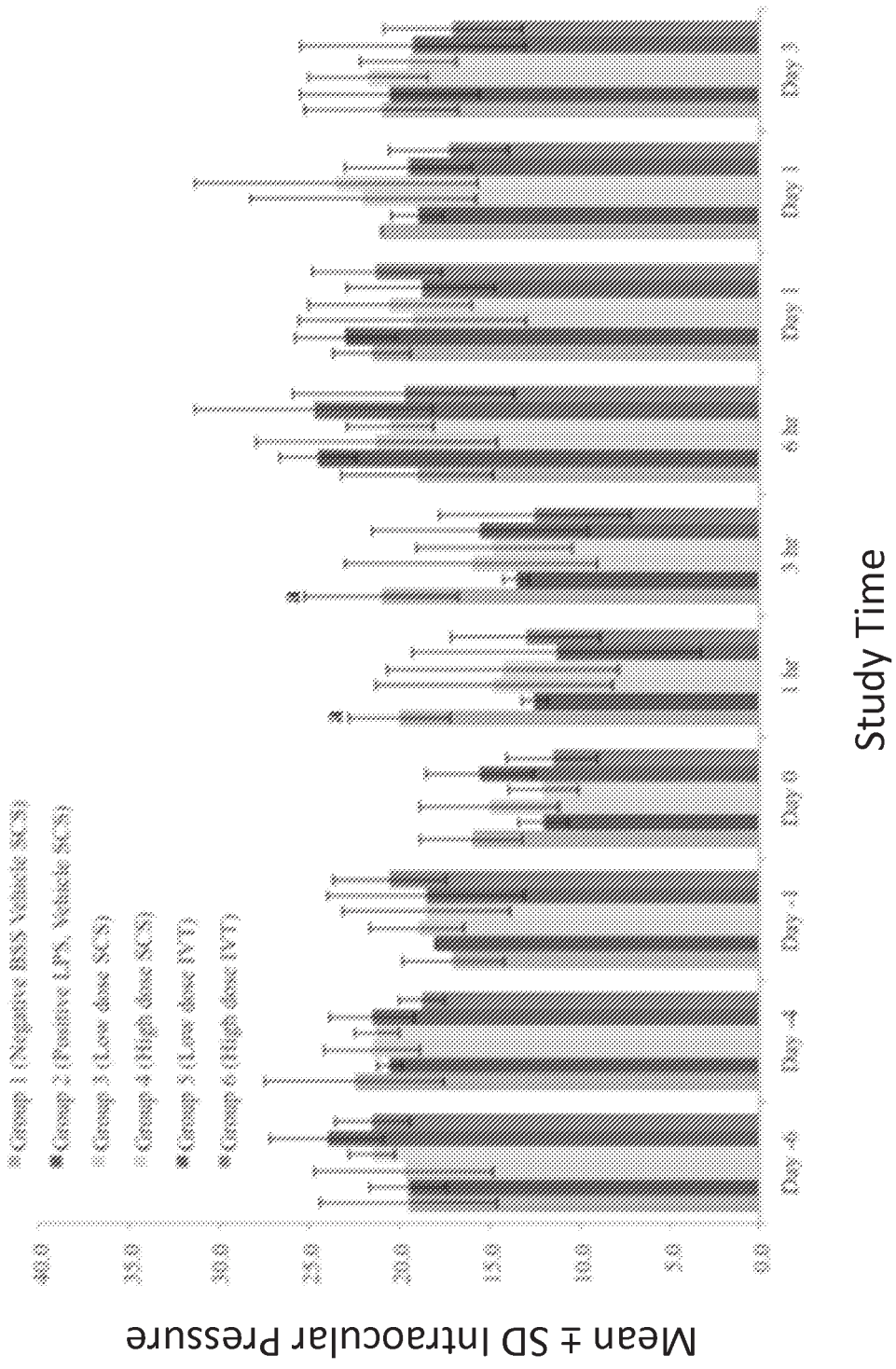

Mean ± SD Intraocular Pressure
Study Time
Group 1 (Negative BSS Vehicle SCS)
Group 2 (Positive LPA, Vehicle SCS)
Group 3 (Low dose SCS)
Group 4 (High dose SCS)
Group 5 (Low dose IVT)
Group 6 (High dose IVT)
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Day -4
Day -4
Day -1
Day 0
1 hr
3 hr
6 hr
Day 1
Day 1
Day 3

FIG. 25A

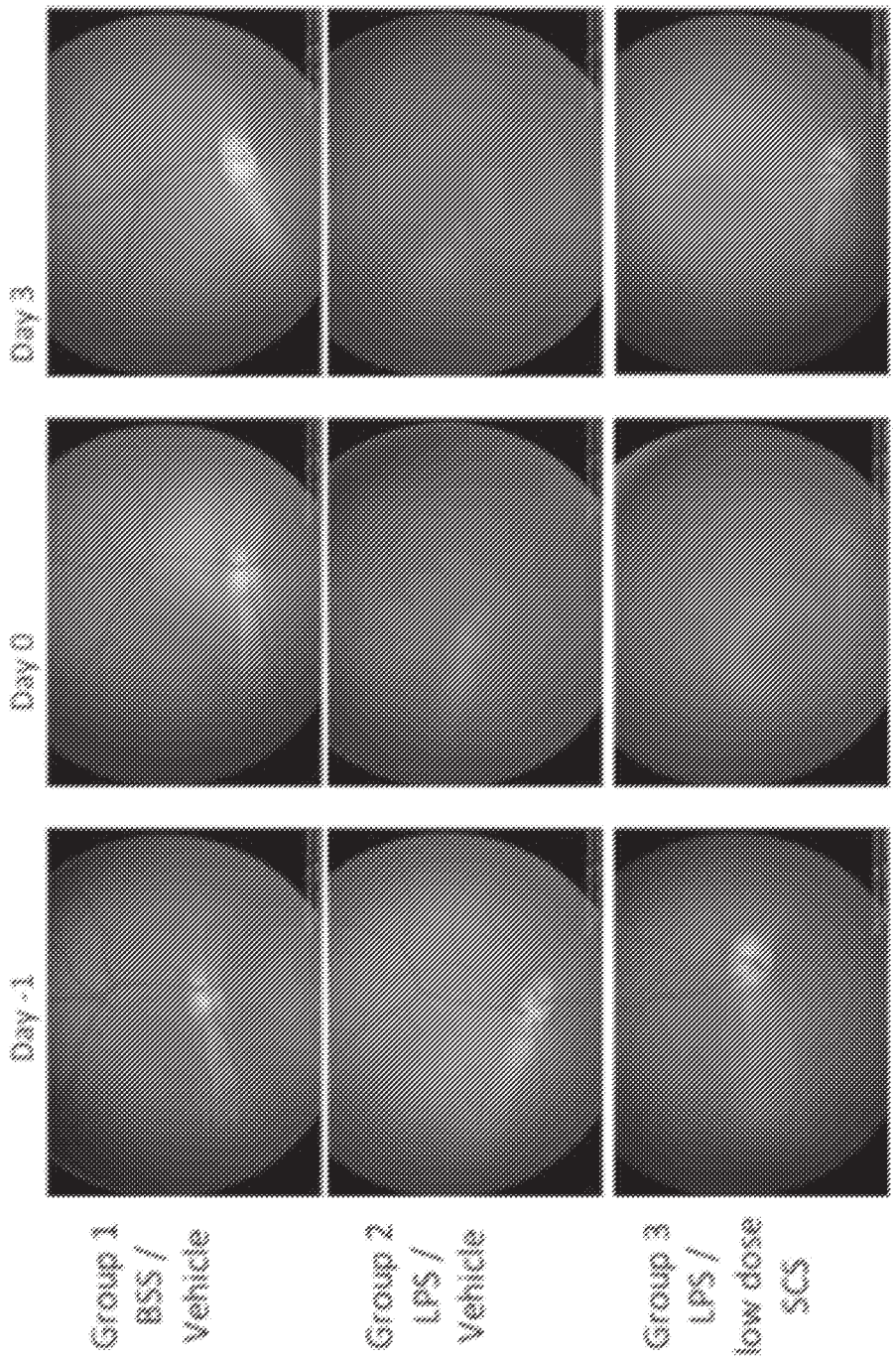

Day -1
Day 0
Day 3
Group 1
BSS /
Vehicle
Group 2
LPS /
Vehicle
Group 3
LPS /
low dose
SCS

FIG. 25B

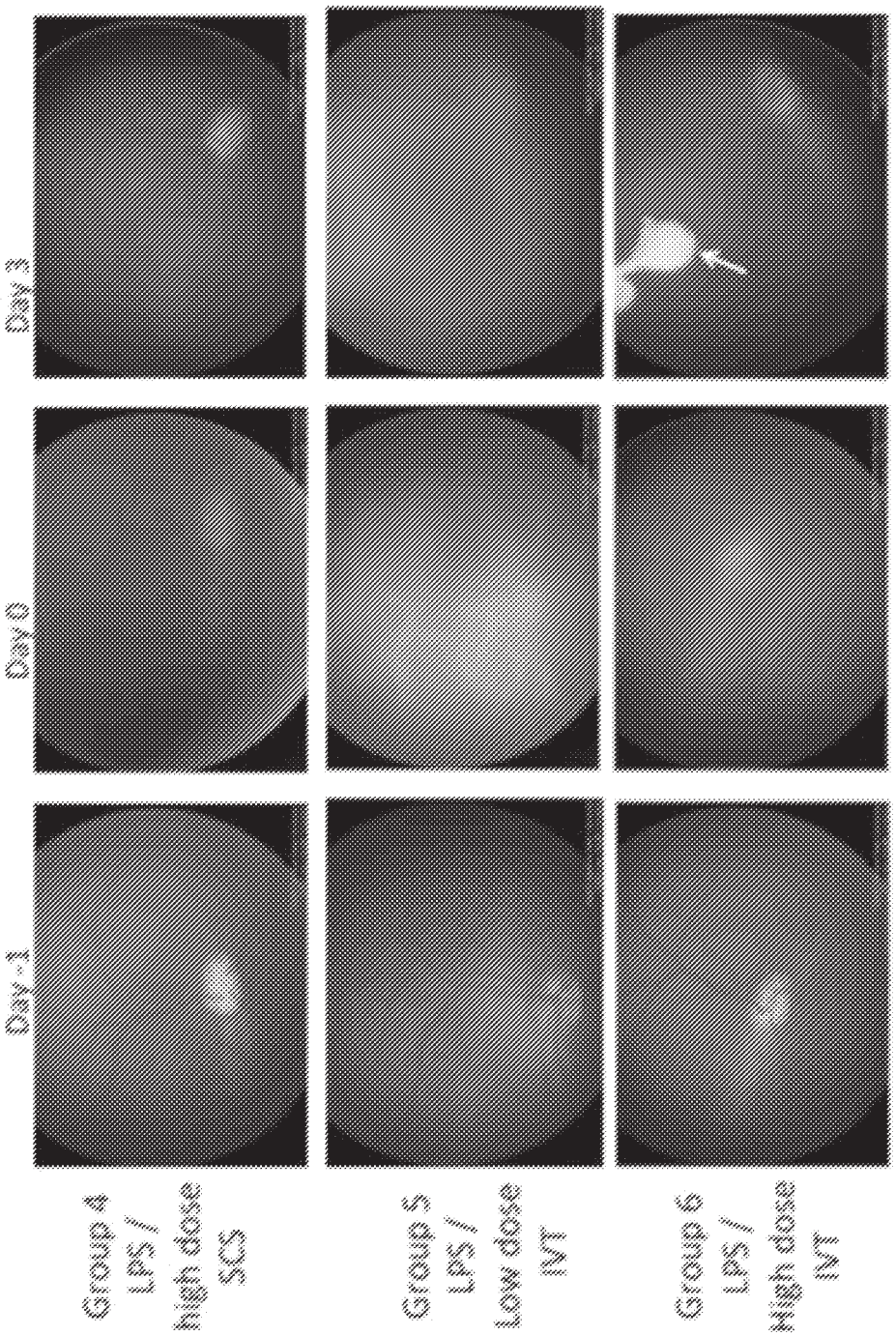

Day -1
Day 0
Day 3
Group 4
LPS /
high dose
SCS
Group 5
LPS /
Low dose
IVT
Group 6
LPS /
High dose
IVT

FIG. 26

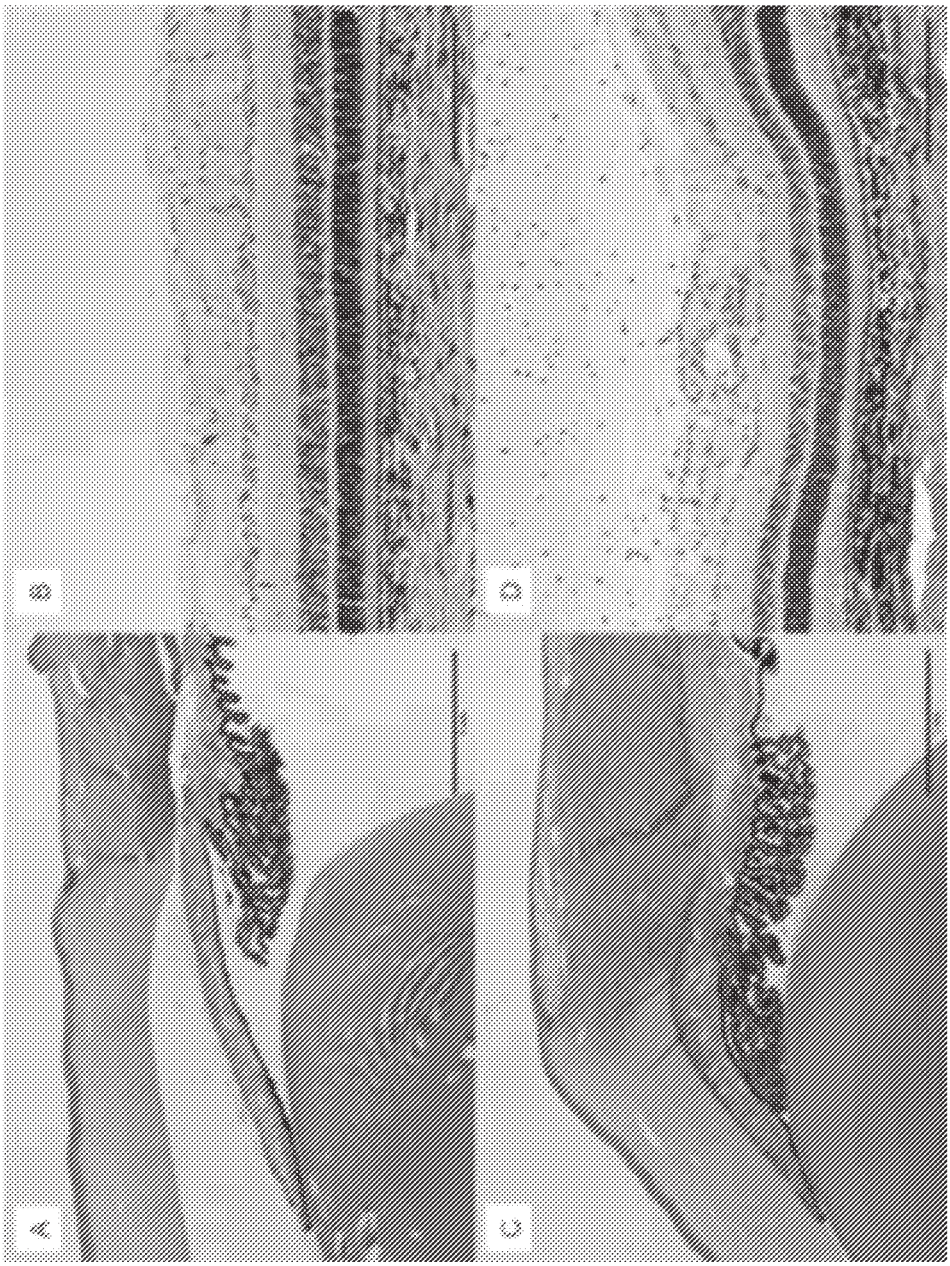


FIG. 26

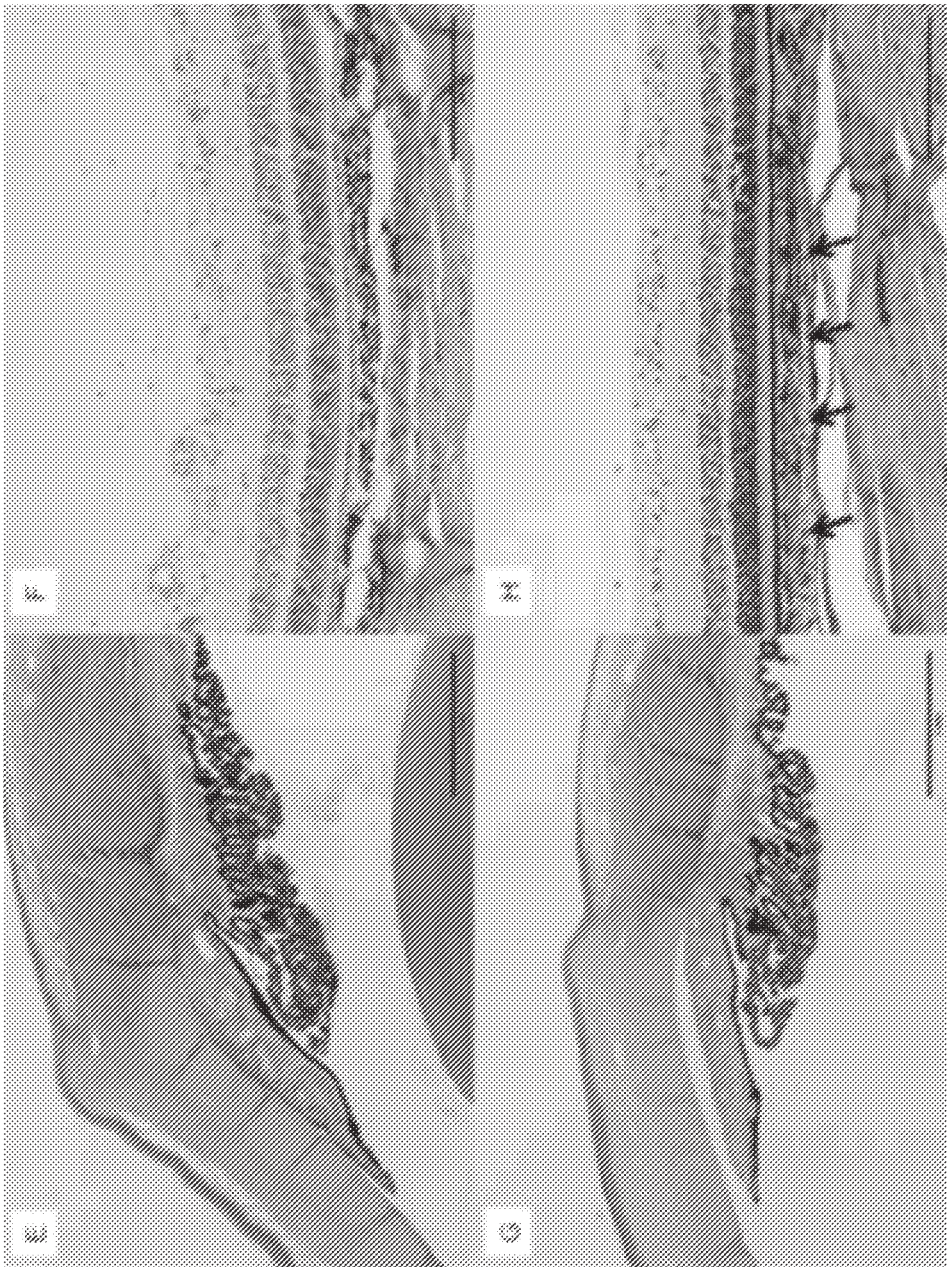


FIG. 26

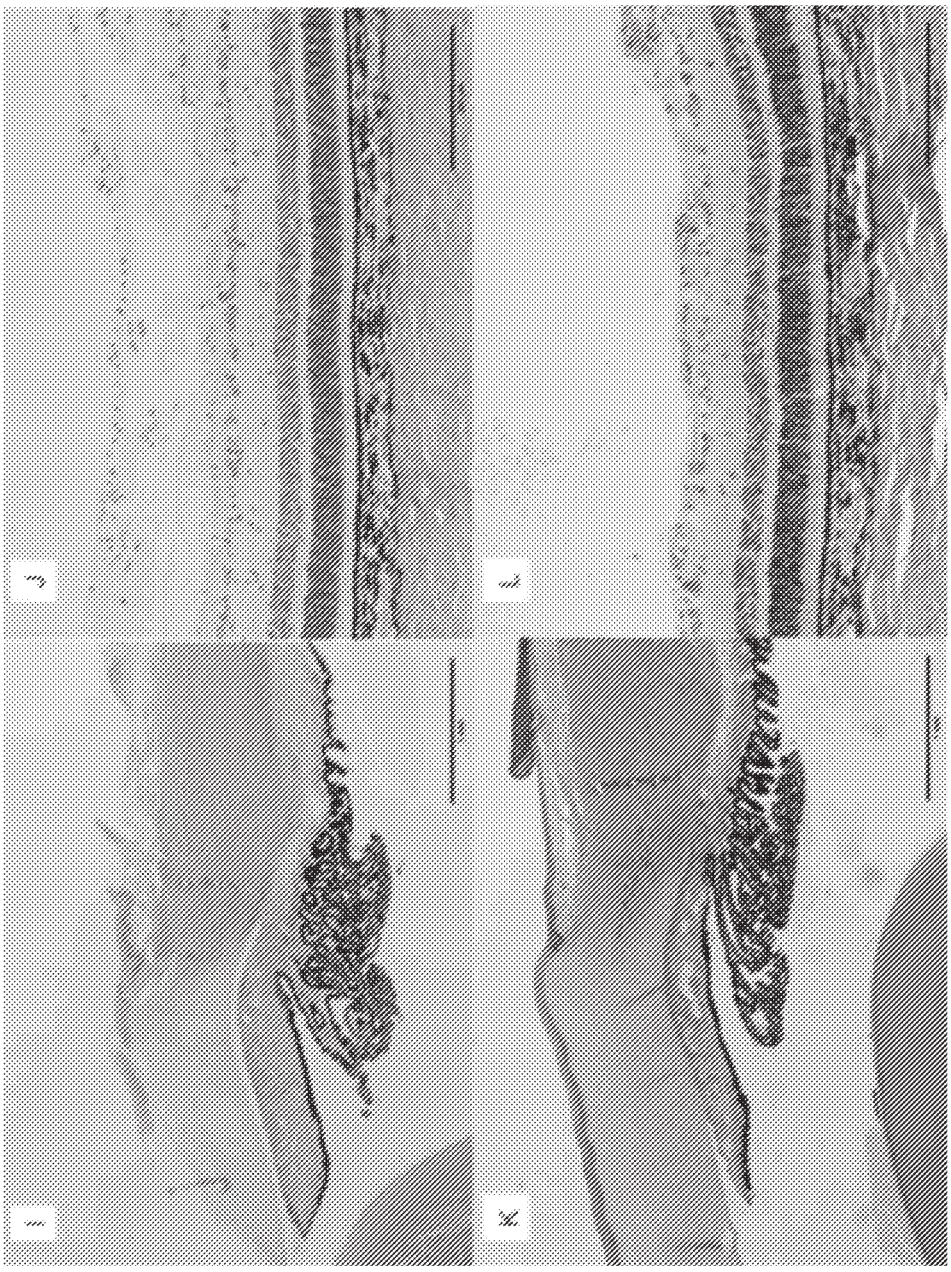


FIG. 27

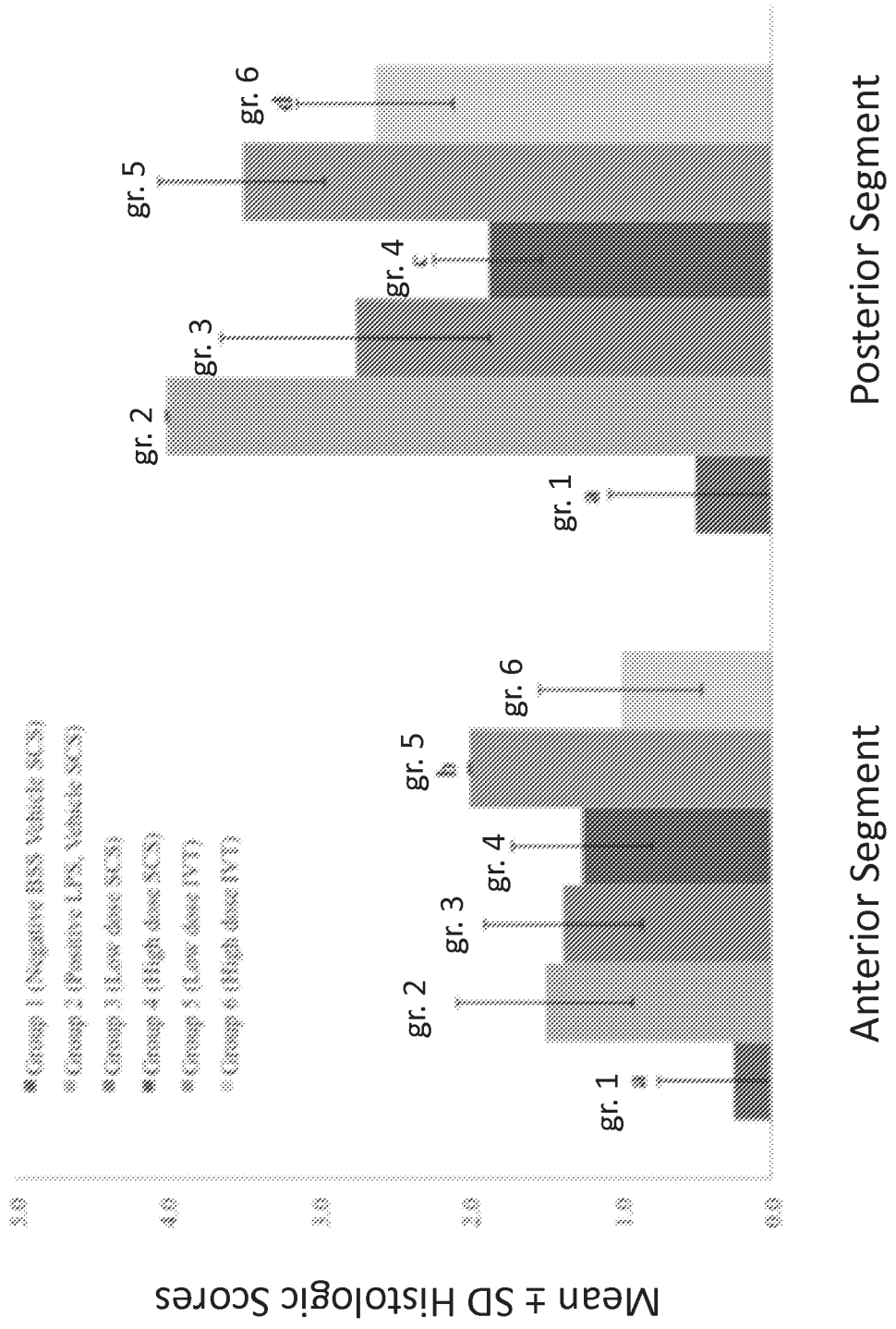

Mean ± SD Histologic Scores
Anterior Segment
Posterior Segment
gr. 1
gr. 2
gr. 3
gr. 4
gr. 5
gr. 6

FIG. 28

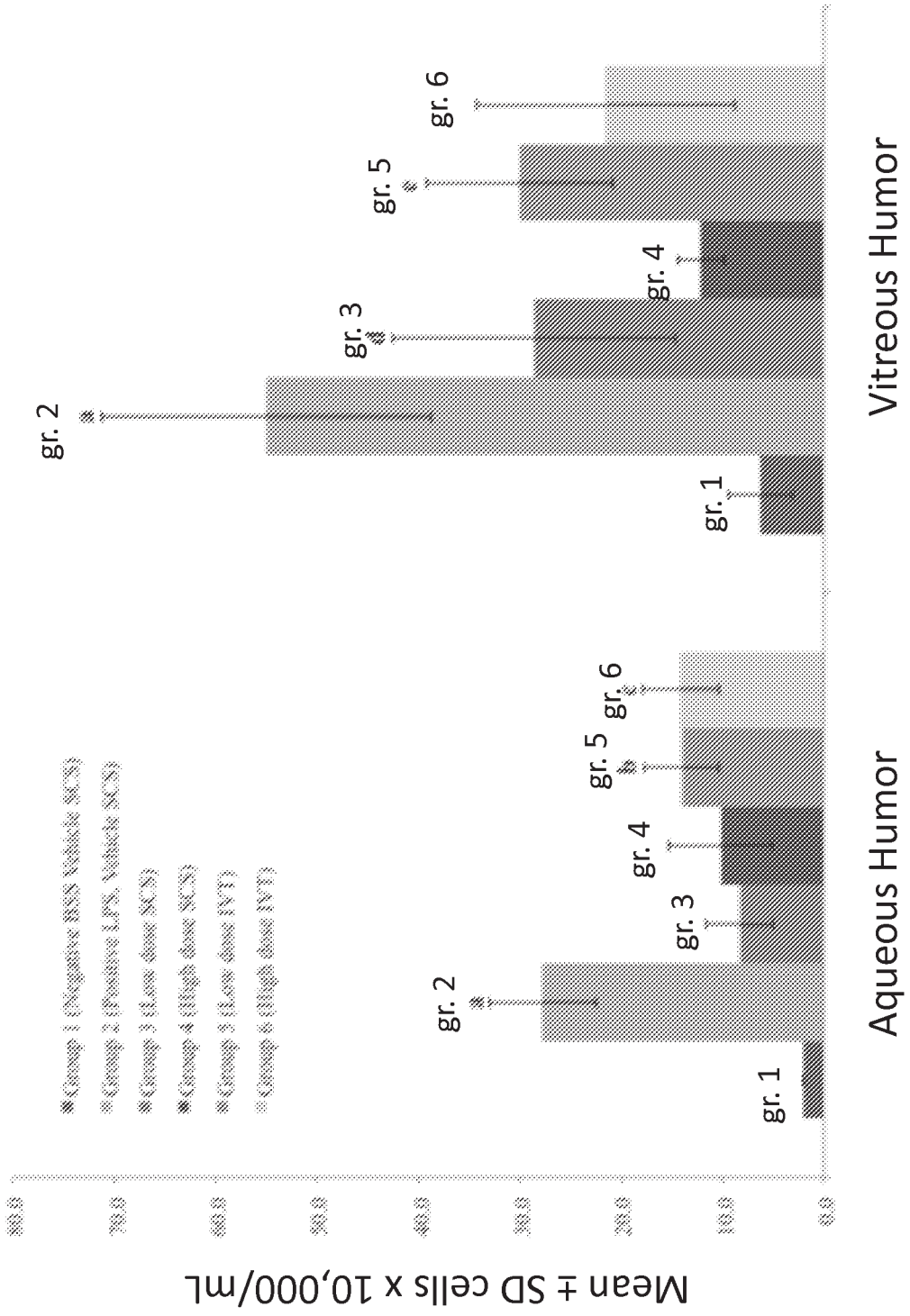
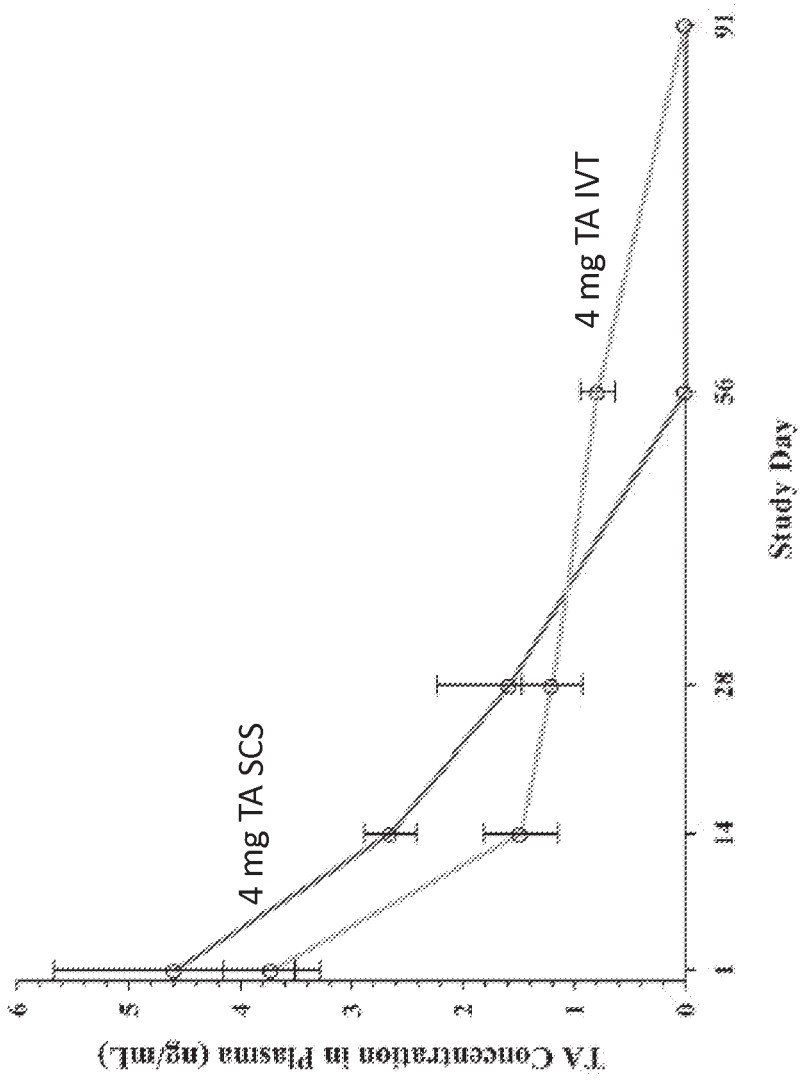
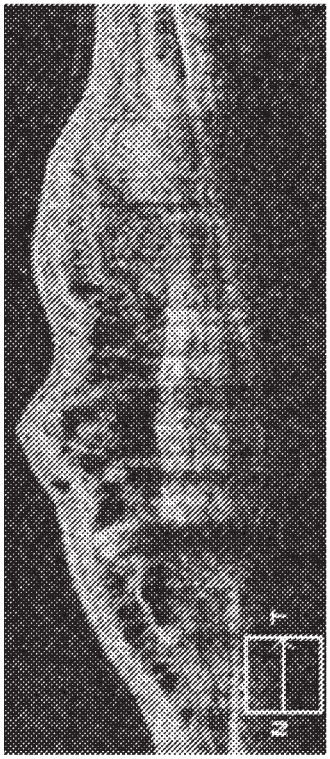

Mean ± SD cells x 10,000/mL
Aqueous Humor
Vitreous Humor
gr. 1
gr. 2
gr. 3
gr. 4
gr. 5
gr. 6

FIG. 29


TA Concentration in Plasma (ng/mL)
0
1
2
3
4
5
6
1
14
28
56
91
Study Day
4 mg TA SCS
4 mg TA IVT



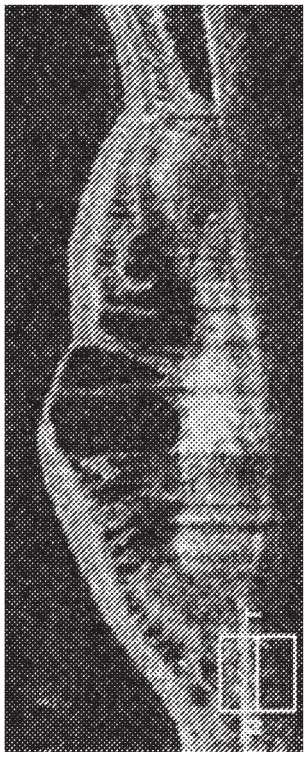


FIG. 30

FIG. 31

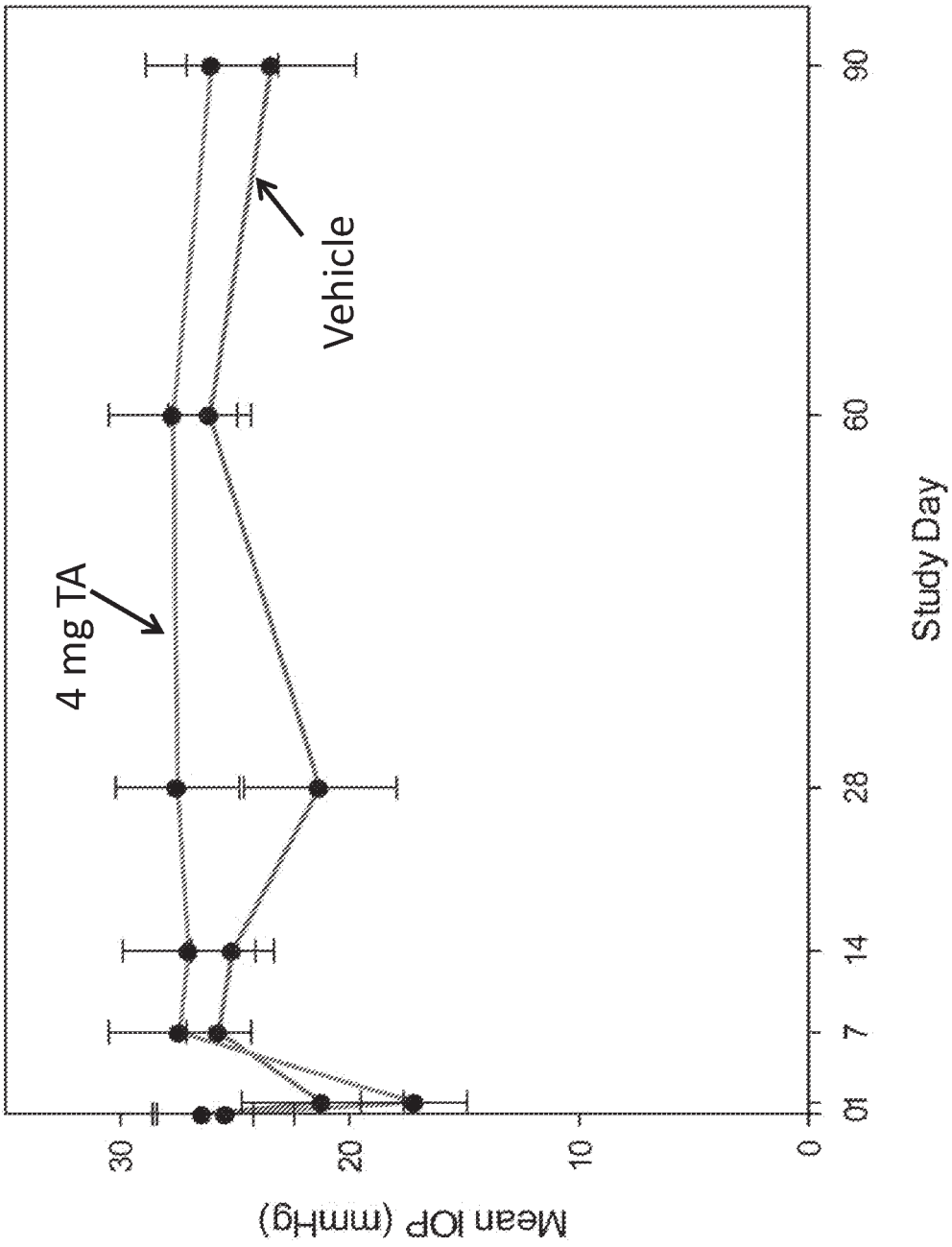


FIG. 32

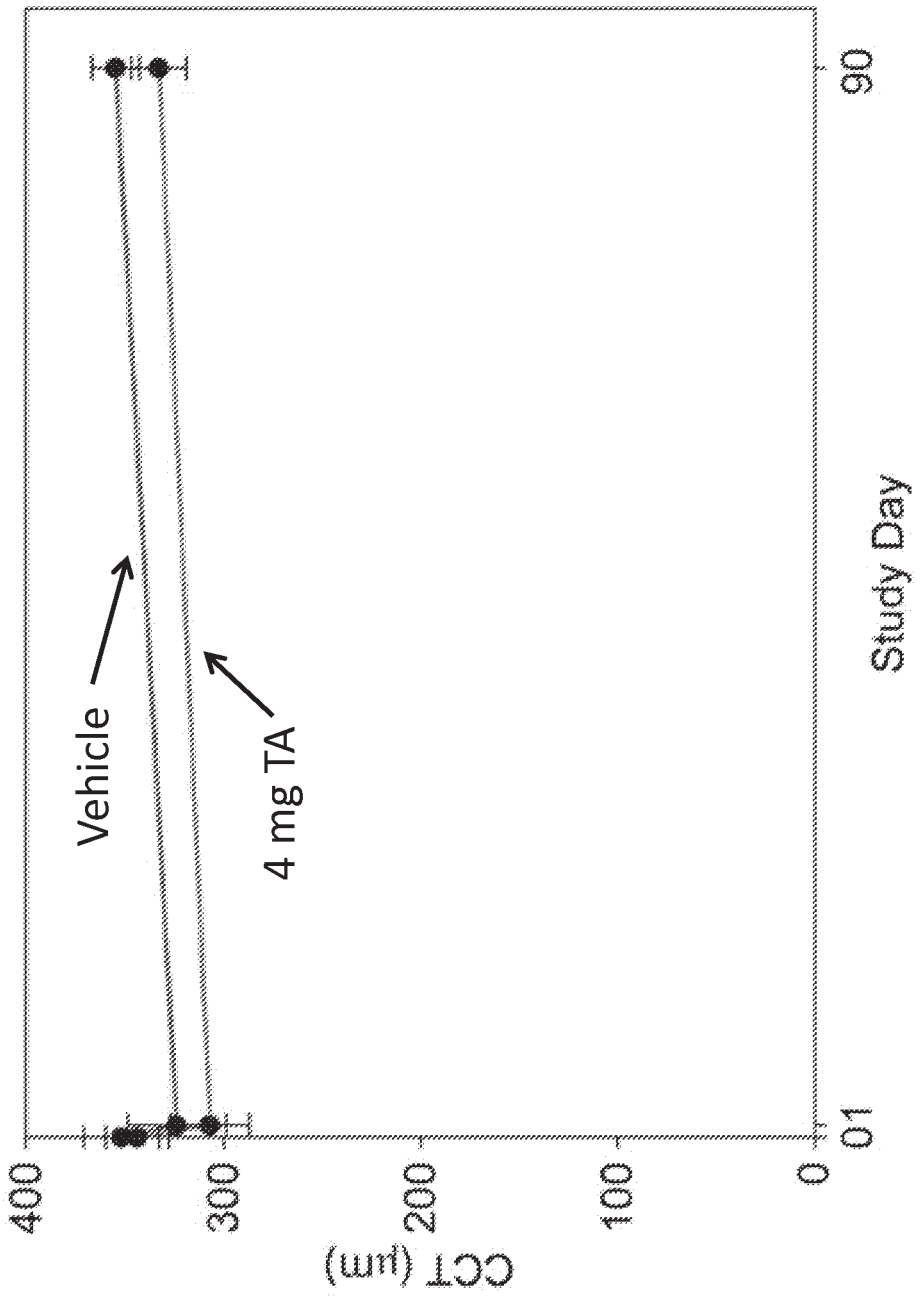
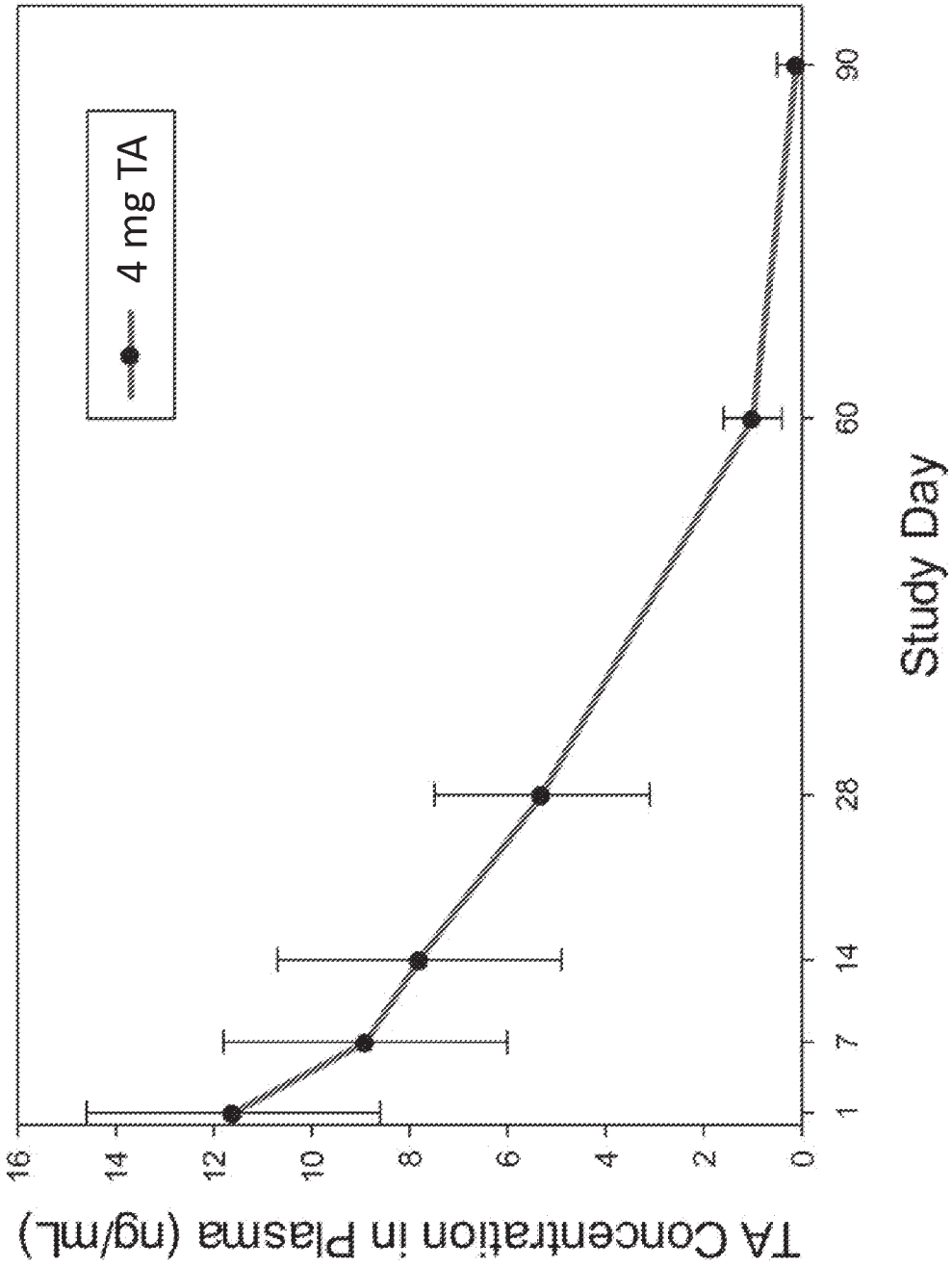


FIG. 33


TA Concentration in Plasma (ng/mL)
0
2
4
6
8
10
12
14
16
1
7
14
28
60
90
Study Day
4 mg TA