FIGURE 1

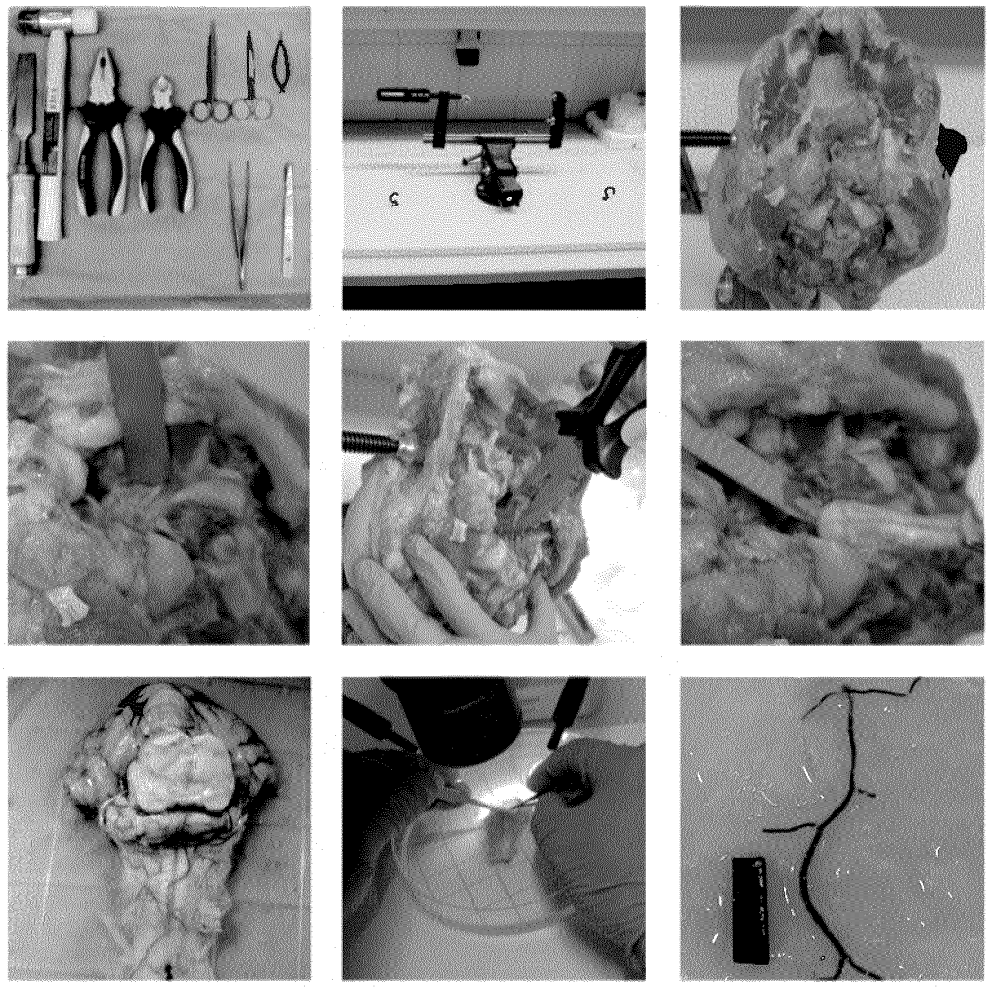
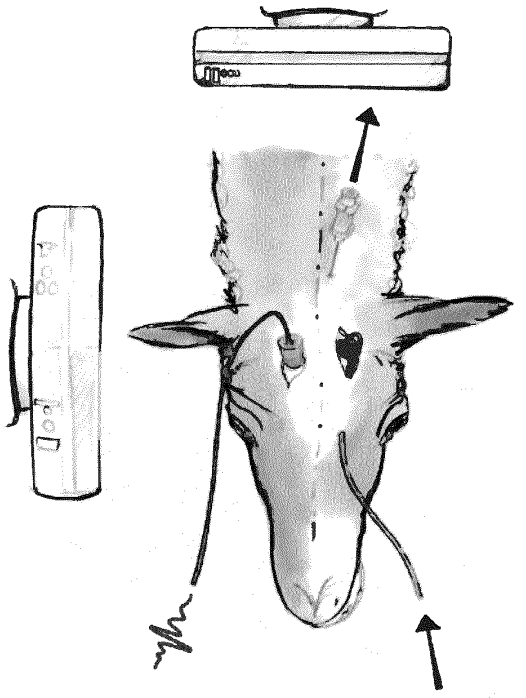


FIGURE 2



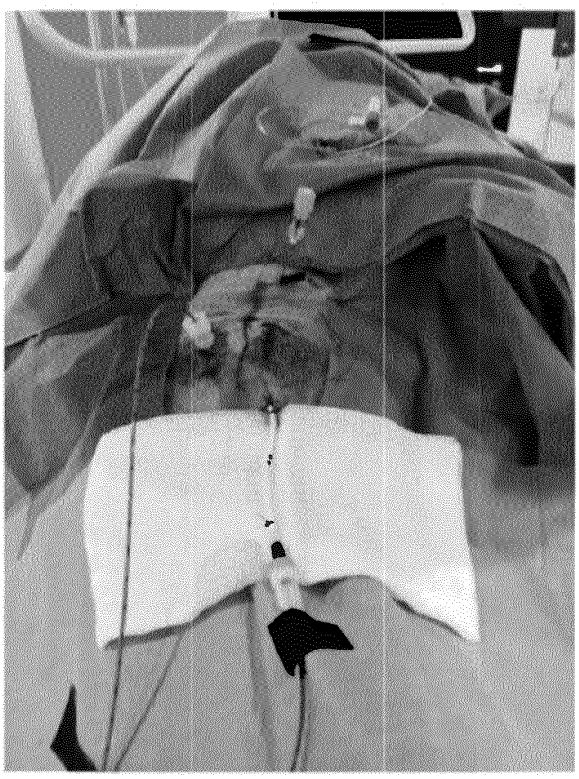


FIGURE 3

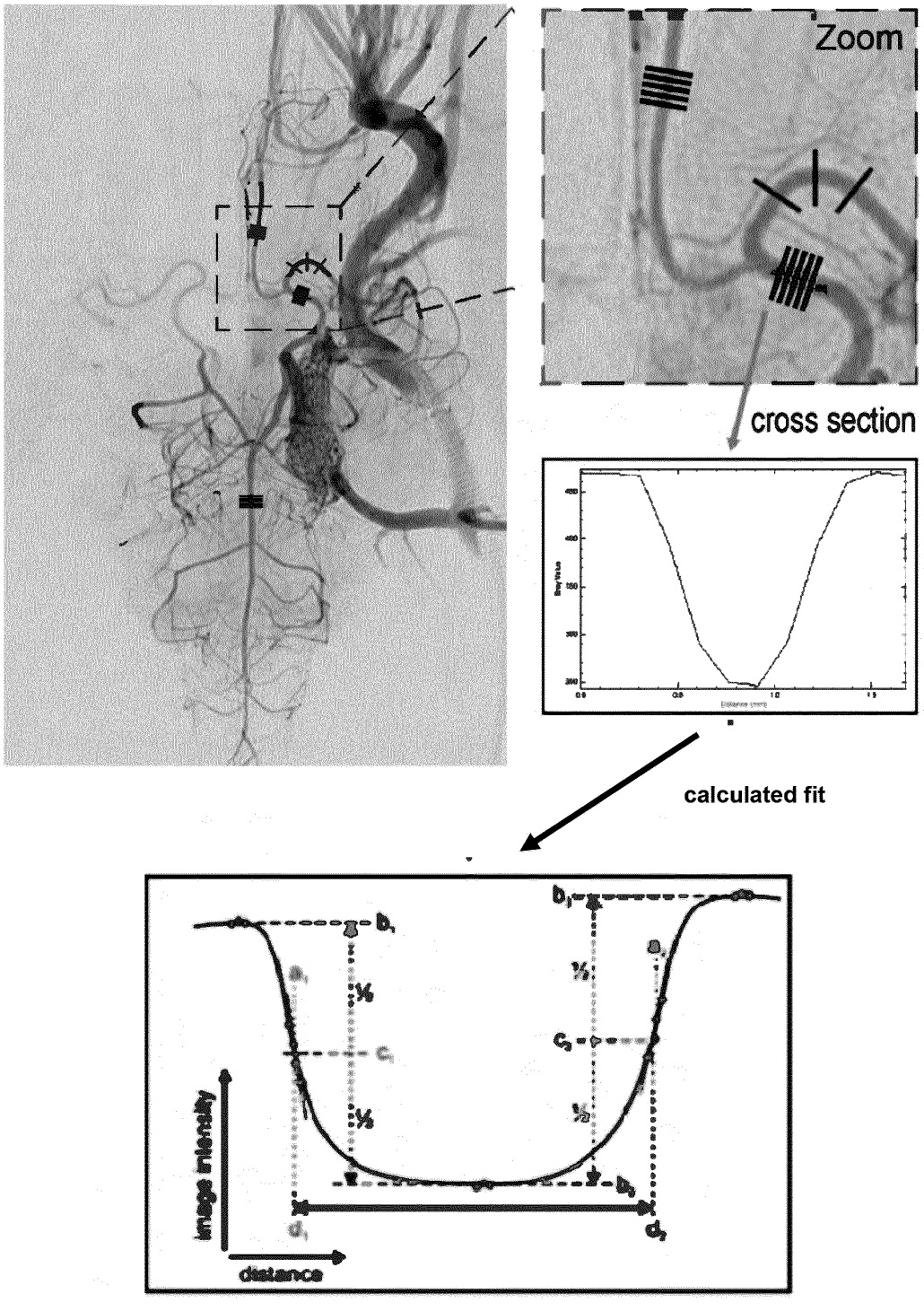
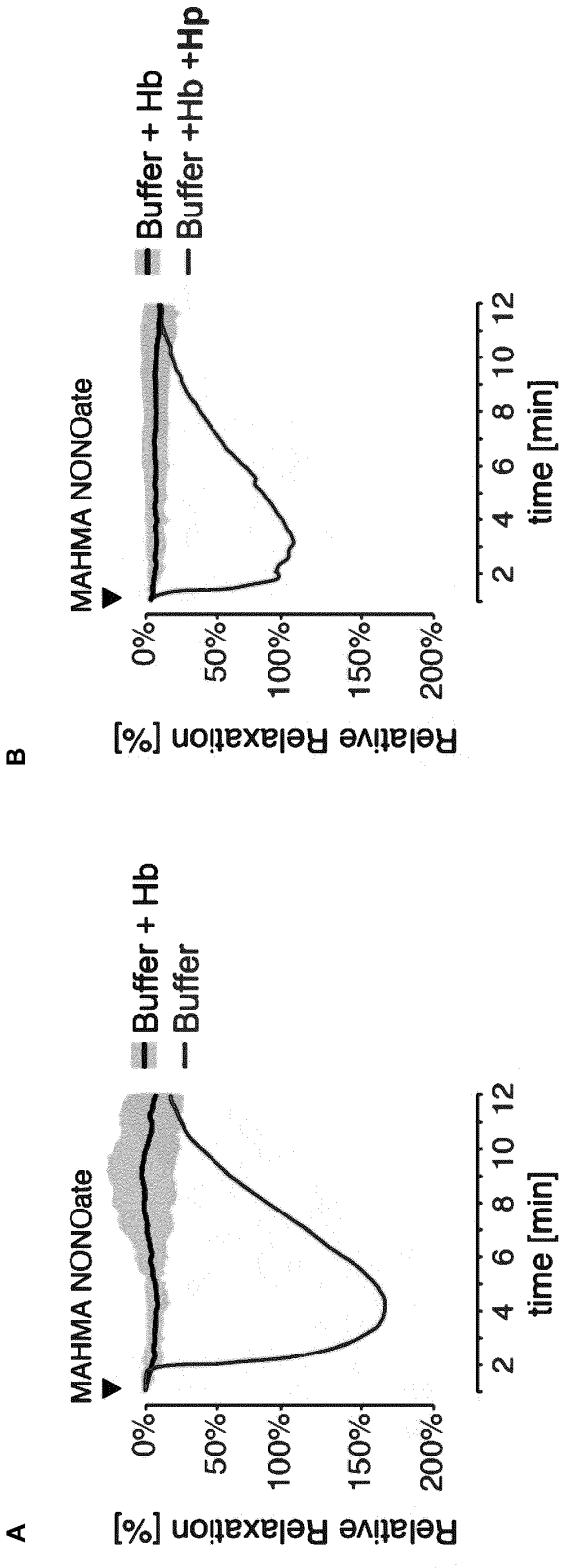

Zoom
cross section
calculated fit
image intensity
distance

FIGURE 4


A
B
MAHMA NONOate
Buffer + Hb
Buffer
Buffer + Hb +Hp
Relative Relaxation [%]
0%
50%
100%
150%
200%
2 4 6 8 10 12
time [min]

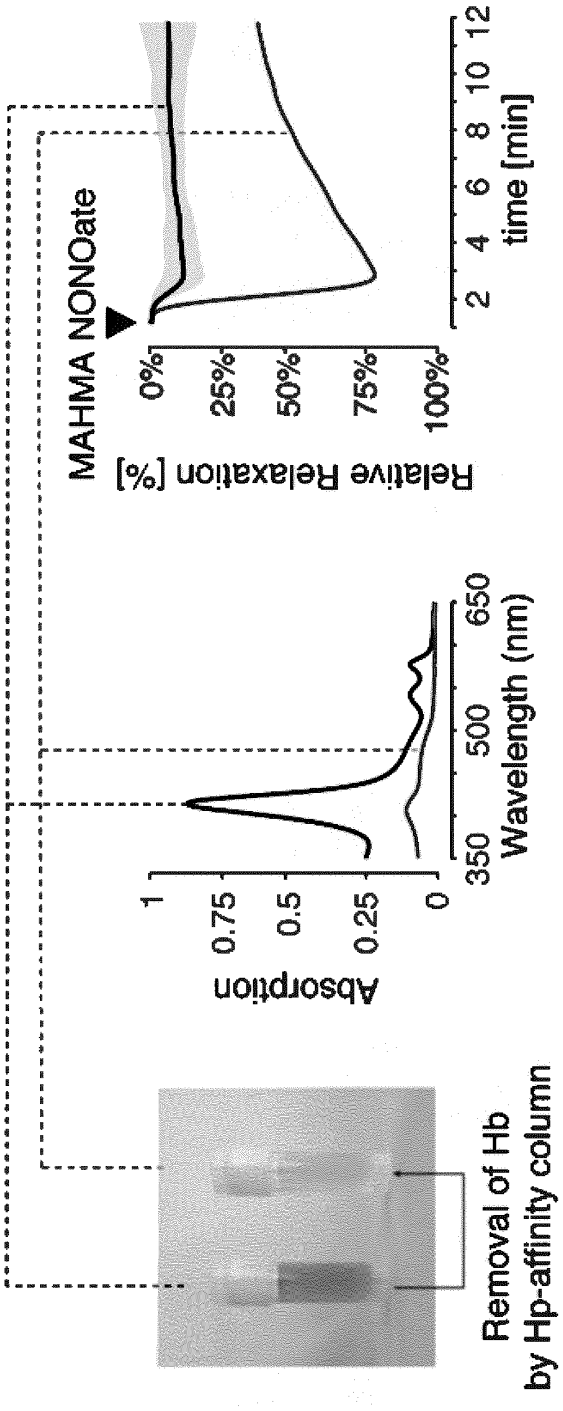

Removal of Hb
by Hp-affinity column
Absorption
1
0.75
0.5
0.25
0
350
500
650
Wavelength (nm)
MAHMA NONOate
Relative Relaxation [%]
0%
25%
50%
75%
100%
2
4
6
8
10
12
time [min]

FIGURE 5

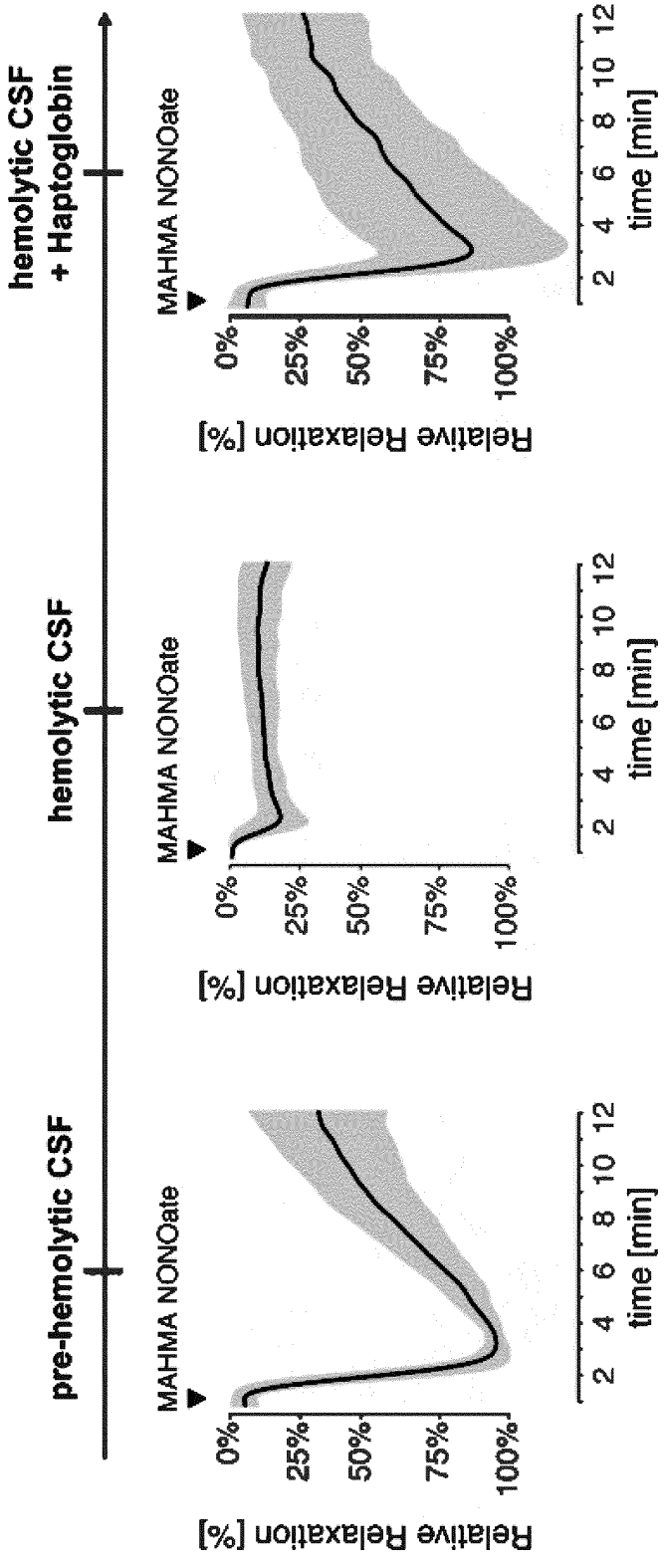

pre-hemolytic CSF
hemolytic CSF
hemolytic CSF
+ Haptoglobin
MAHMA NONOate
Relative Relaxation [%]
0%
25%
50%
75%
100%
2 4 6 8 10 12
time [min]

FIGURE 6

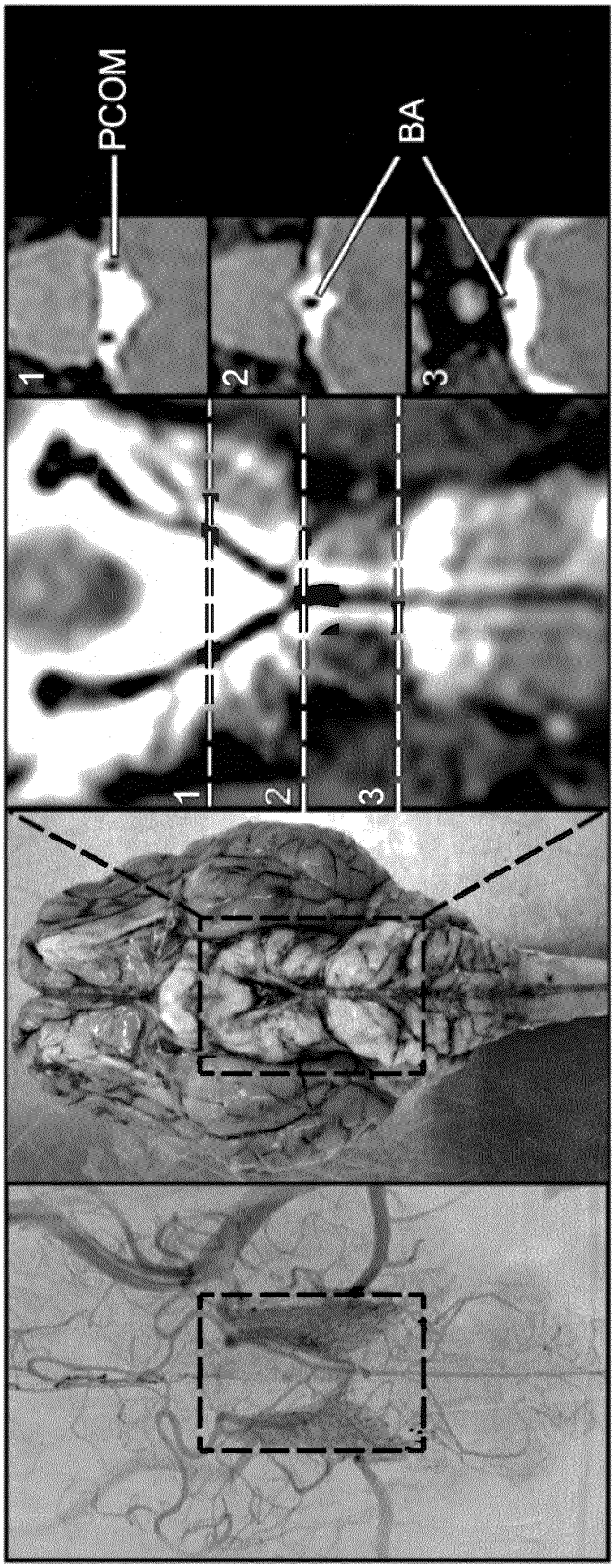


FIGURE 7

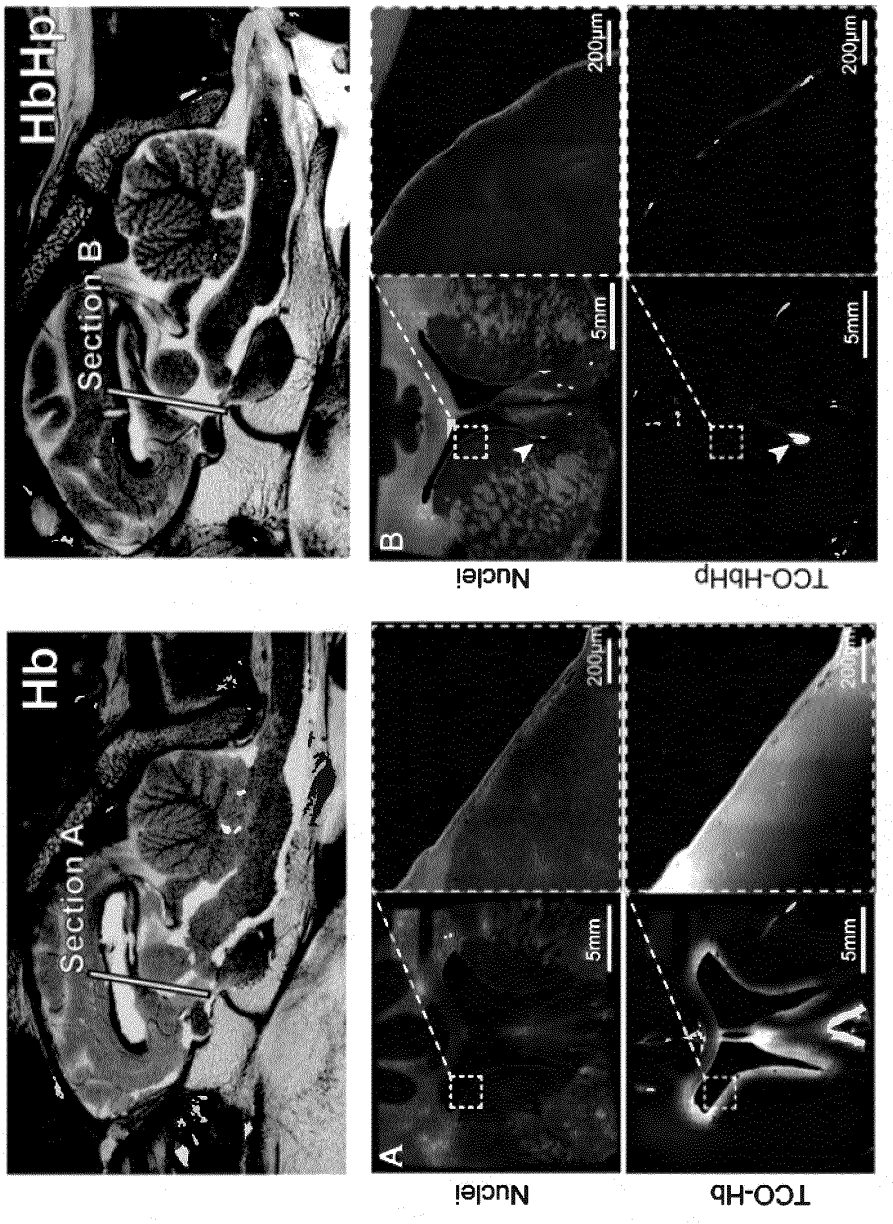

Hb
Section A
HbHp
Section B
A
B
Nuclei
TCO-Hb
TCO-HbHp
5mm
200µm

FIGURE 8

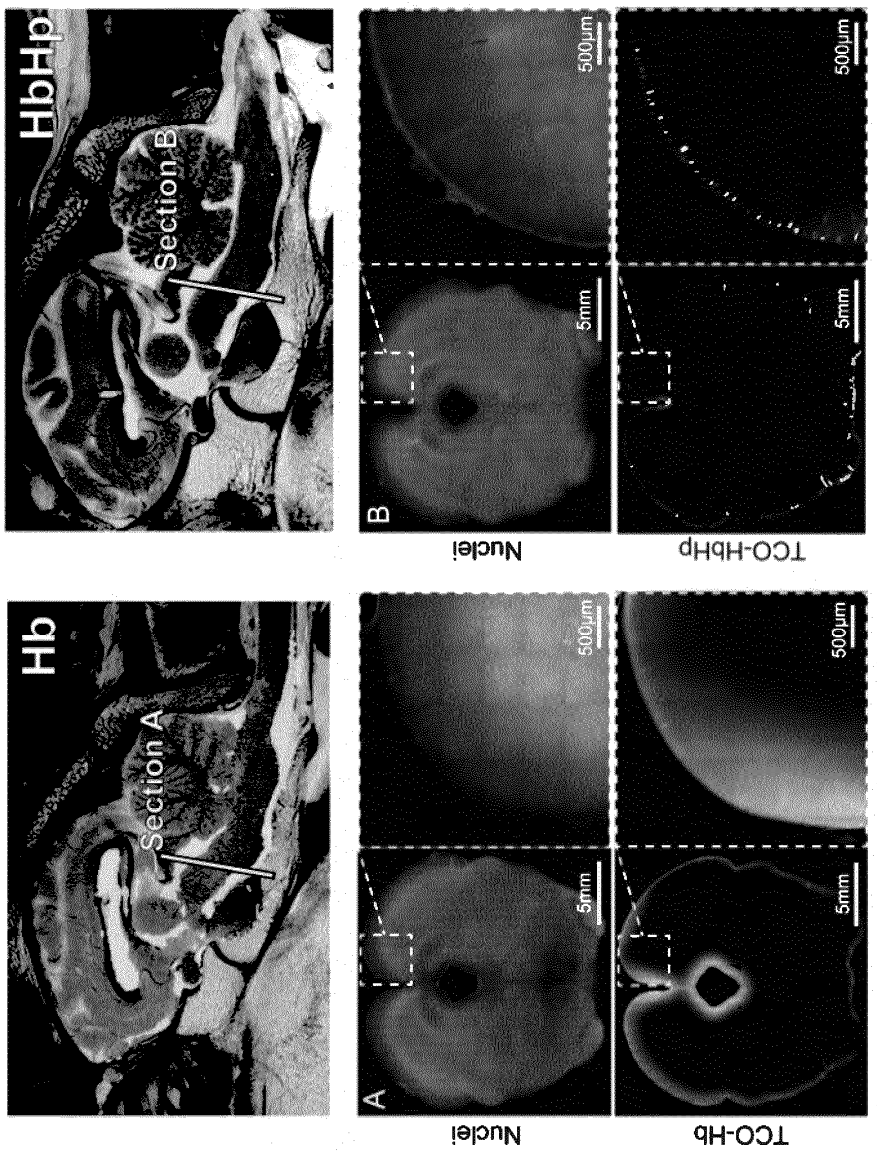

Hb
Section A
HbHp
Section B
A
B
Nuclei
TCO-Hb
TCO-HbHp
5mm
500µm

FIGURE 9

FIGURE 10

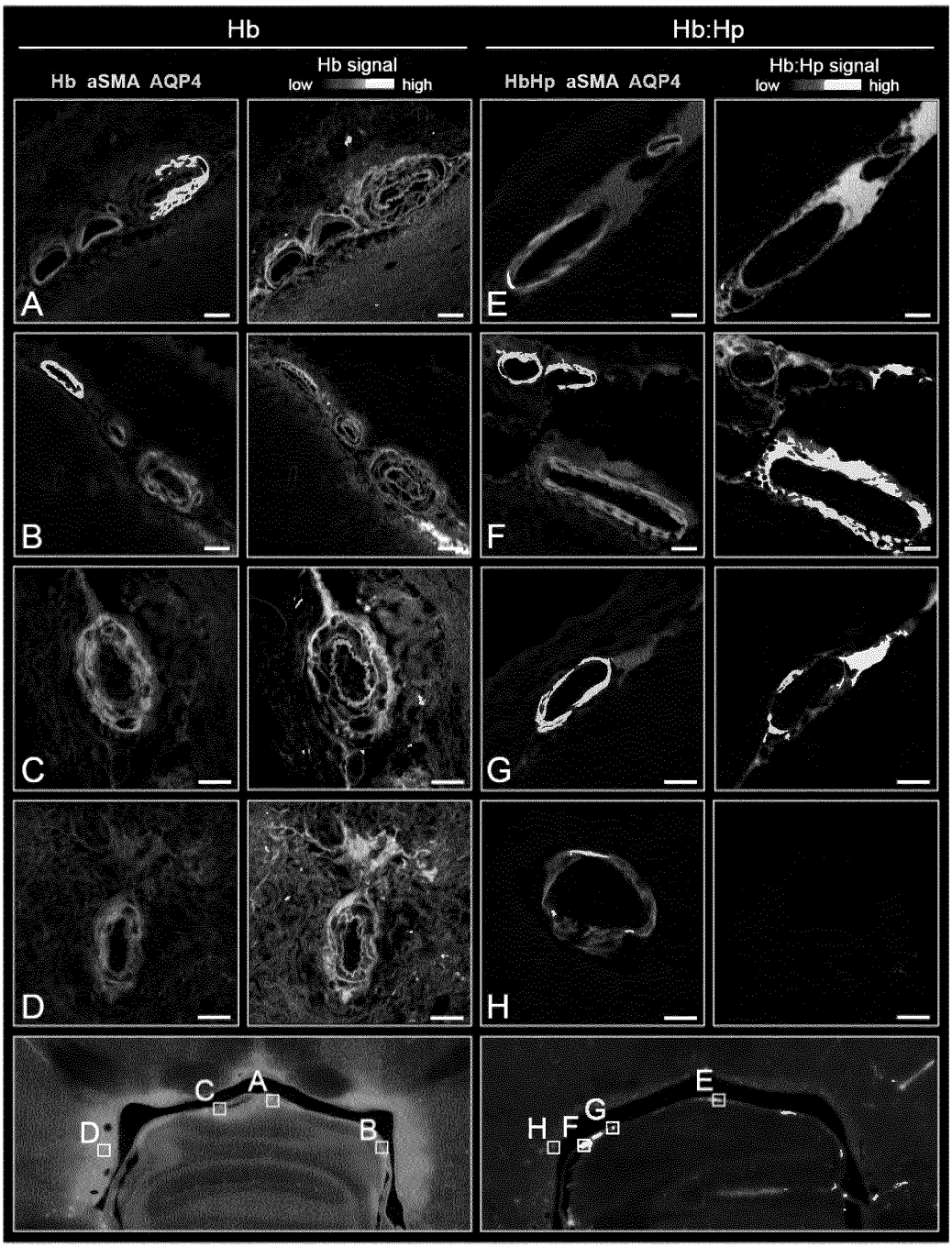

Hb
Hb:Hp
Hb aSMA AQP4
Hb signal
low
high
HbHp aSMA AQP4
Hb:Hp signal
low
high
A
B
C
D
E
F
G
H
C
A
D
B
E
G
H
F

FIGURE 11

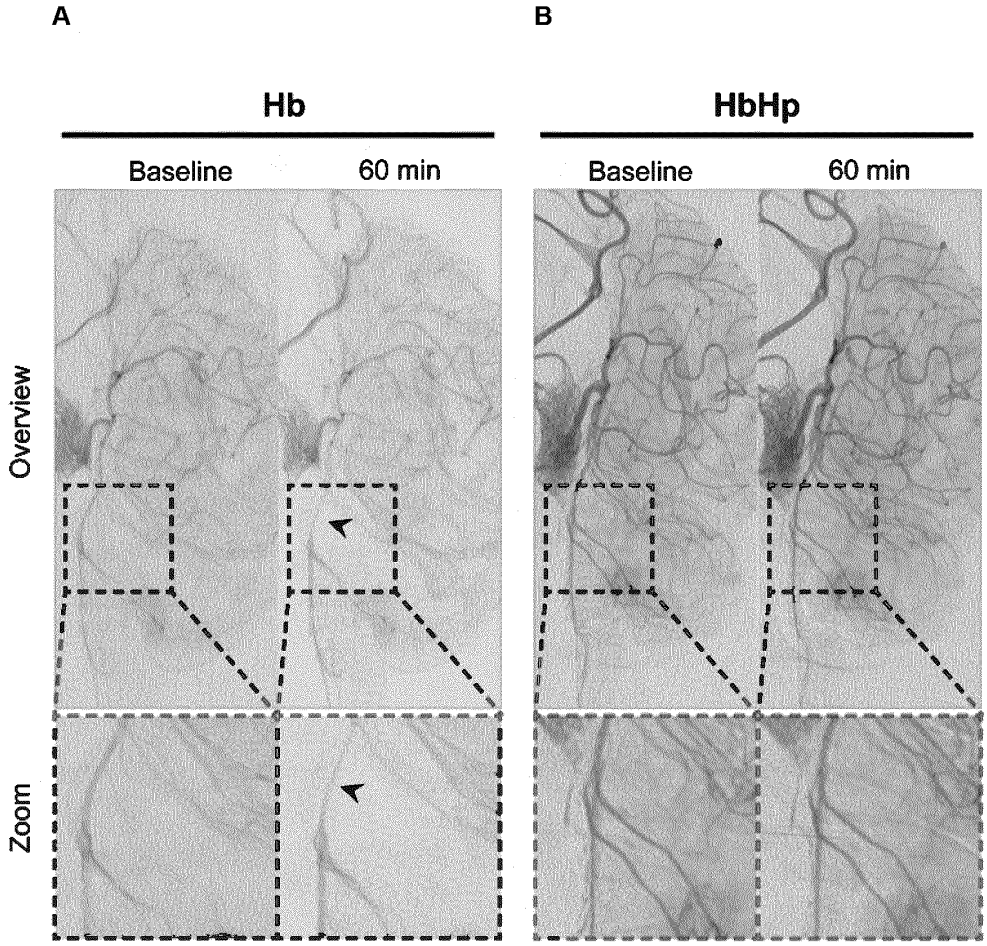
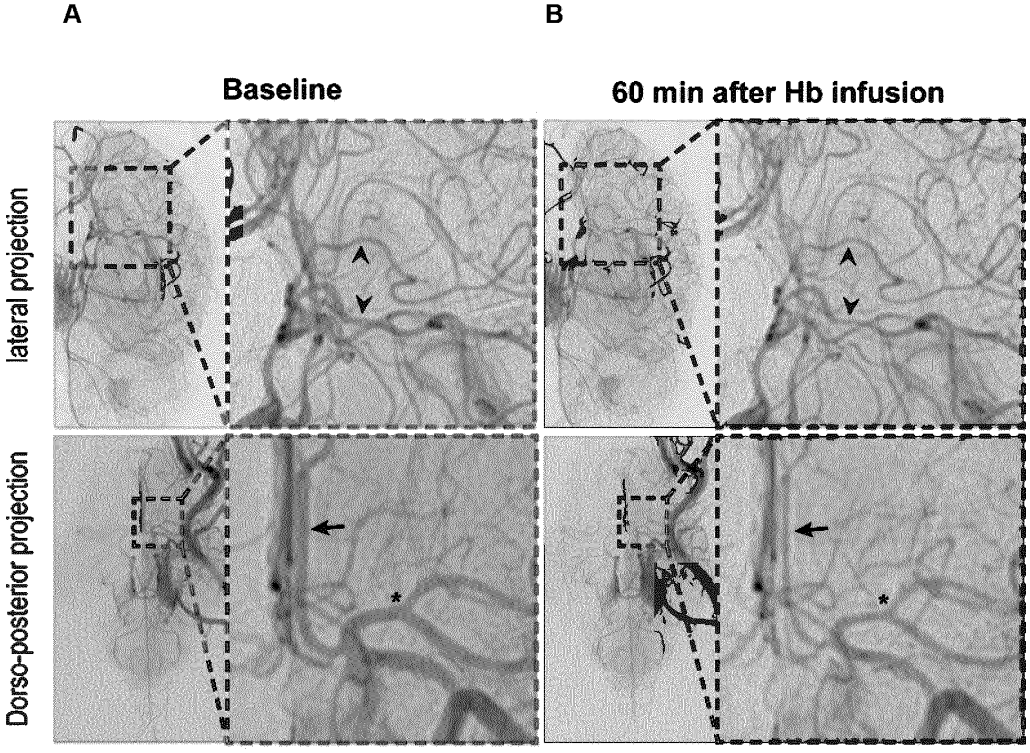


FIGURE 12


A
B
Baseline
60 min after Hb infusion
lateral projection
Dorso-posterior projection

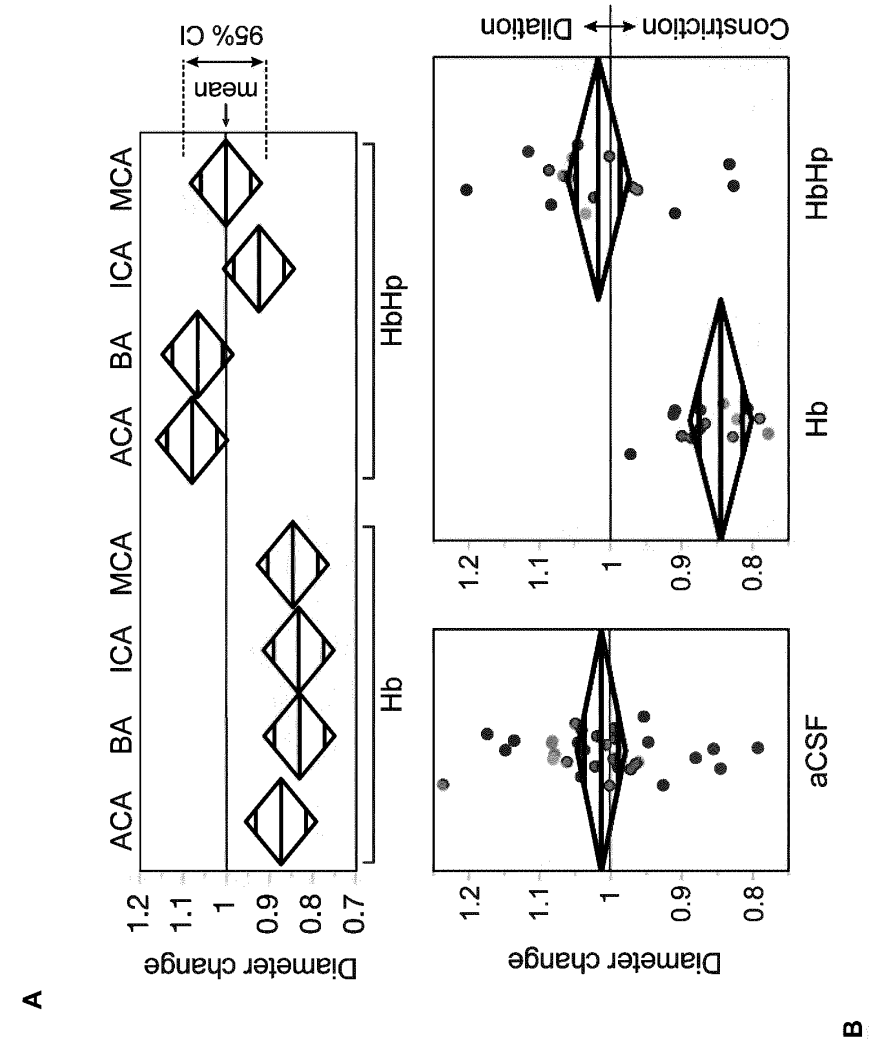

A
ACA
BA
ICA
MCA
ACA
BA
ICA
MCA
Hb
HbHp
mean
95% CI
Diameter change
1.2
1.1
1
0.9
0.8
0.7
B
aCSF
Hb
HbHp
Diameter change
Constriction
Dilation
C

FIGURE 13

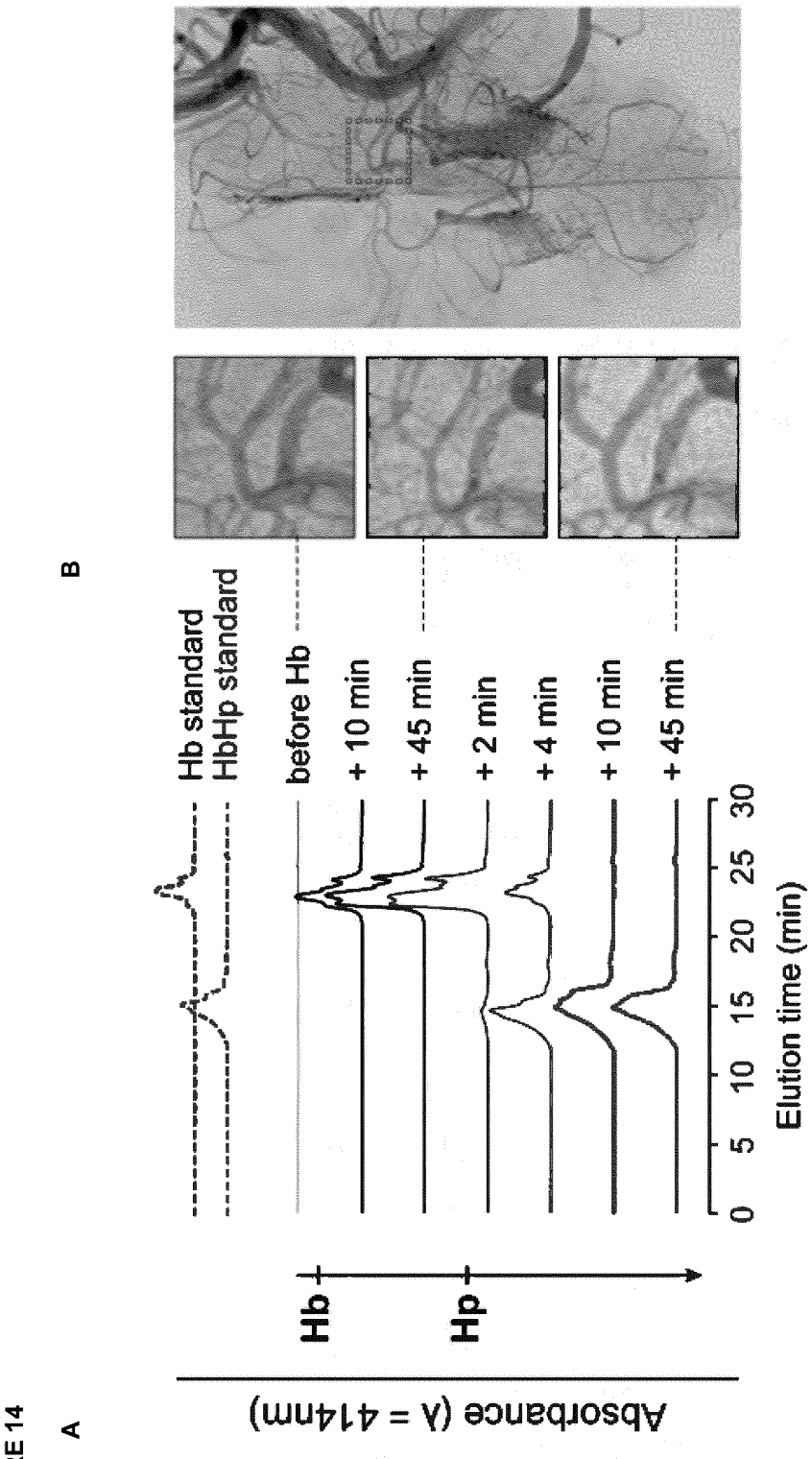

A
B
Absorbance (λ = 414nm)
Hb
Hp
Hb standard
HbHp standard
before Hb
+ 10 min
+ 45 min
+ 2 min
+ 4 min
+ 10 min
+ 45 min
0
5
10
15
20
25
30
Elution time (min)

FIGURE 14

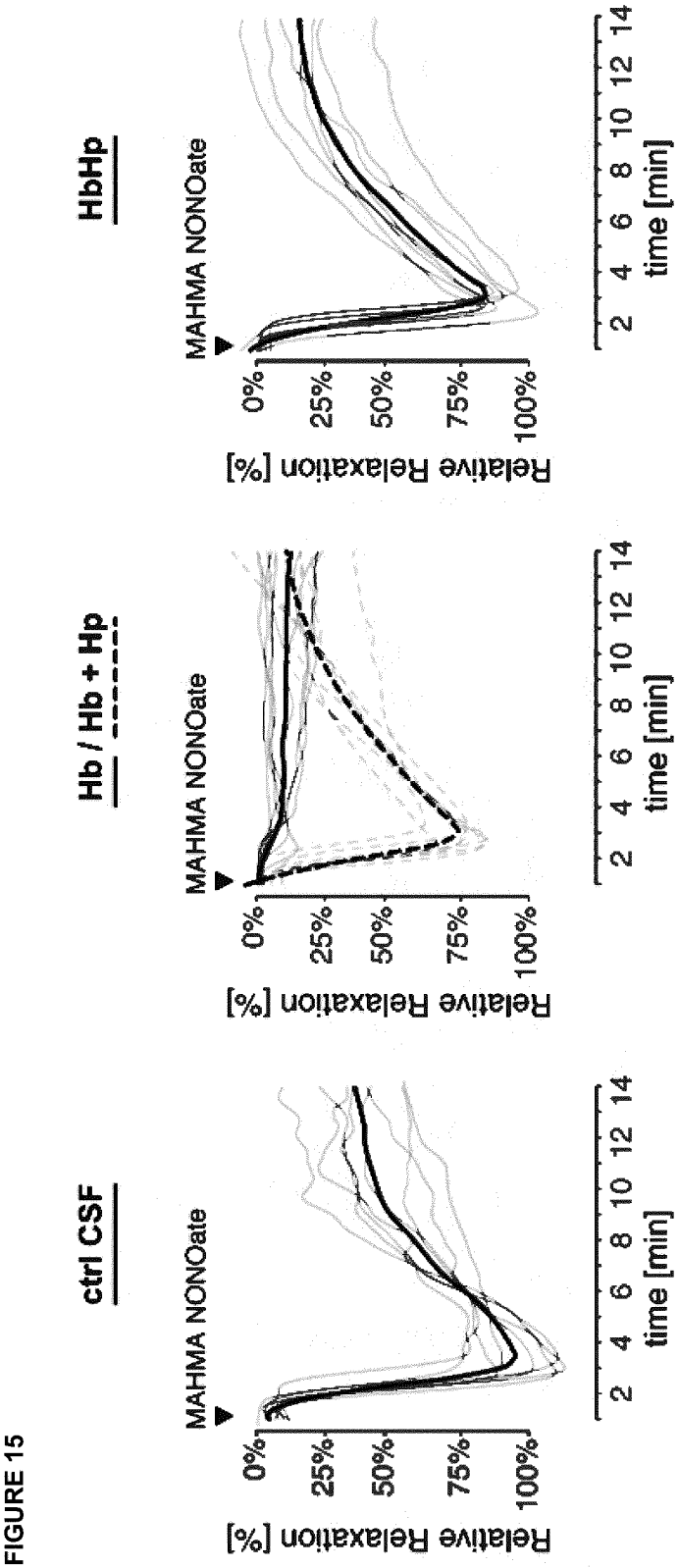

ctrl CSF
Hb / Hb + Hp
HbHp
MAHMA NONOate
Relative Relaxation [%]
0%
25%
50%
75%
100%
2 4 6 8 10 12 14
time [min]

FIGURE 15

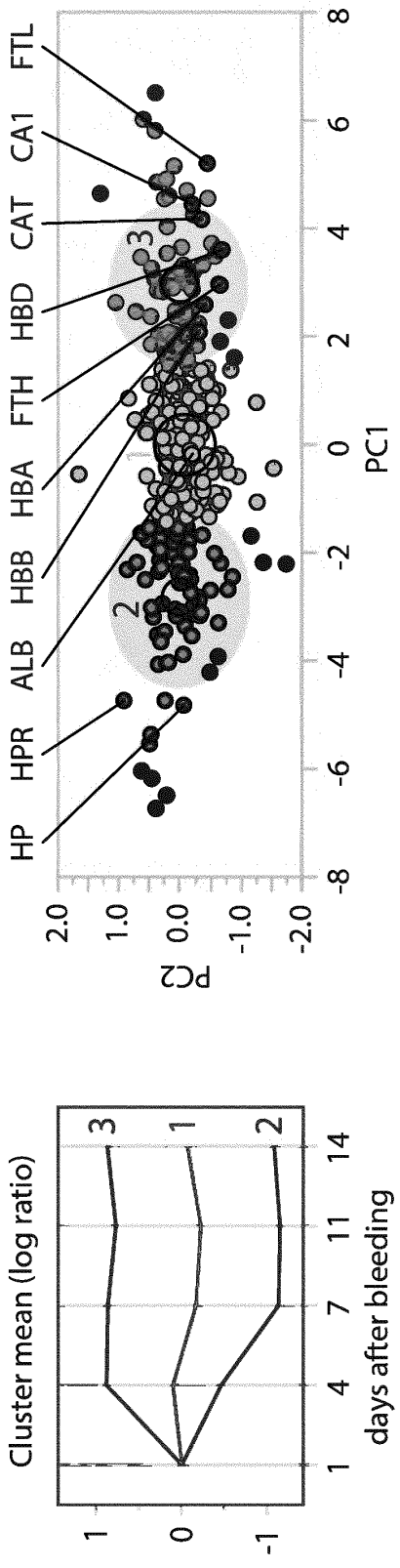

HP
HPR
ALB
HBB
HBA
FTH
HBD
CAT
CA1
FTL
1
2
3
PC2
PC1
2.0
1.0
0.0
-1.0
-2.0
8
6
4
2
0
-2
-4
-6
-8
Cluster mean (log ratio)
1
0
-1
1
4
7
11
14
days after bleeding

FIGURE 16

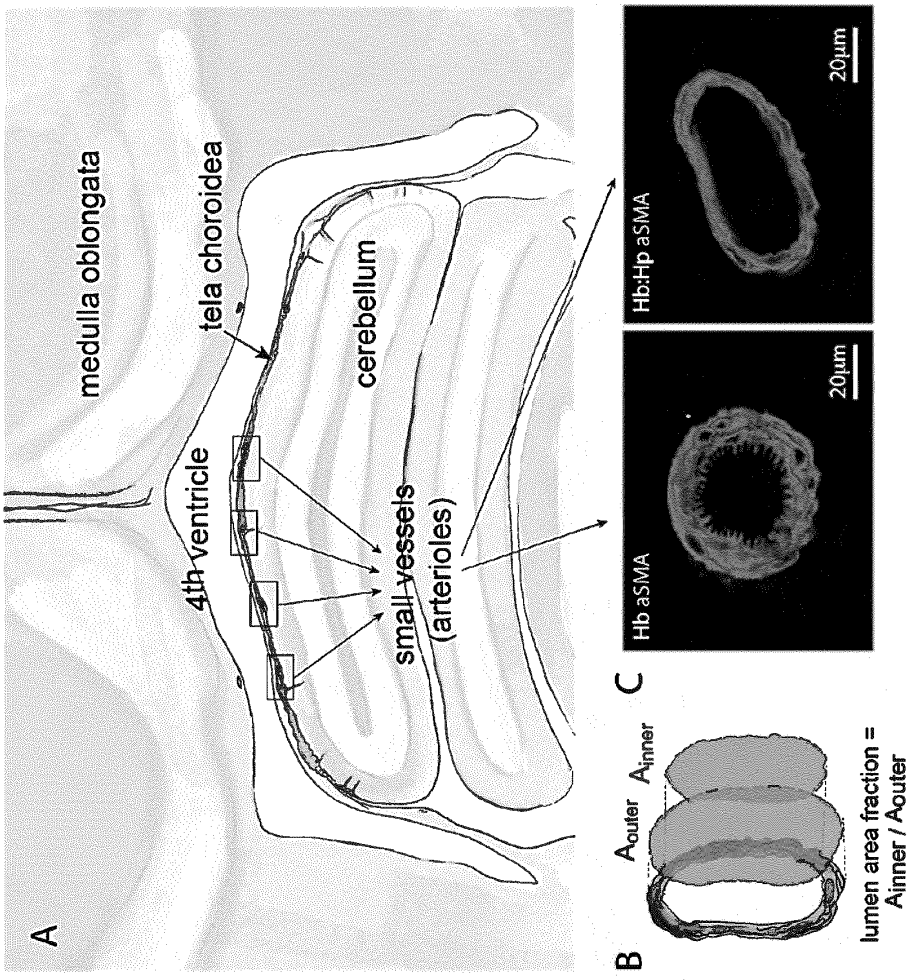

A
medulla oblongata
tela choroidea
4th ventricle
cerebellum
small vessels
(arterioles)
B
Aouter
Ainner
lumen area fraction =
Ainner / Aouter
C
Hb aSMA
20µm
Hb:Hp aSMA
20µm

FIGURE 17

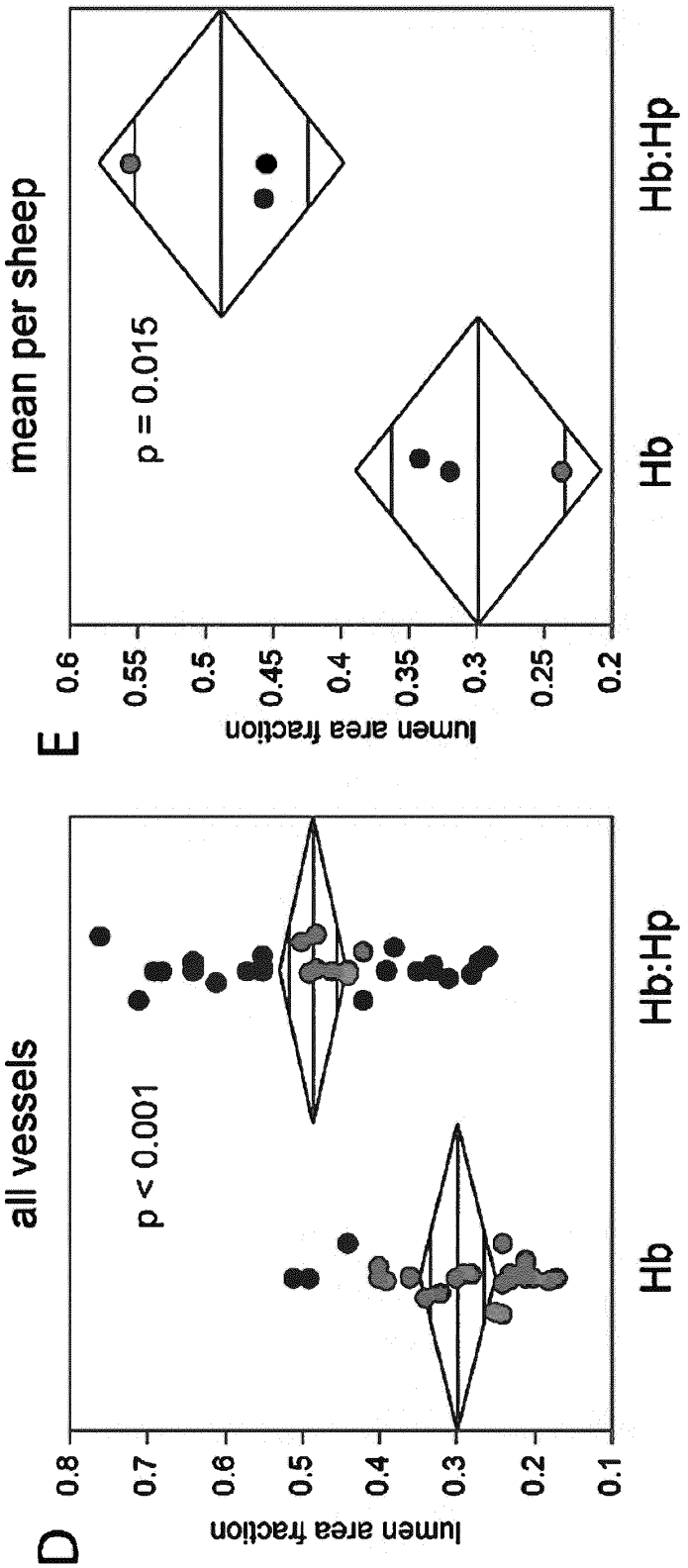

D
all vessels
p < 0.001
lumen area fraction
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Hb
Hb:Hp
E
mean per sheep
p = 0.015
lumen area fraction
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
Hb
Hb:Hp

FIGURE 17

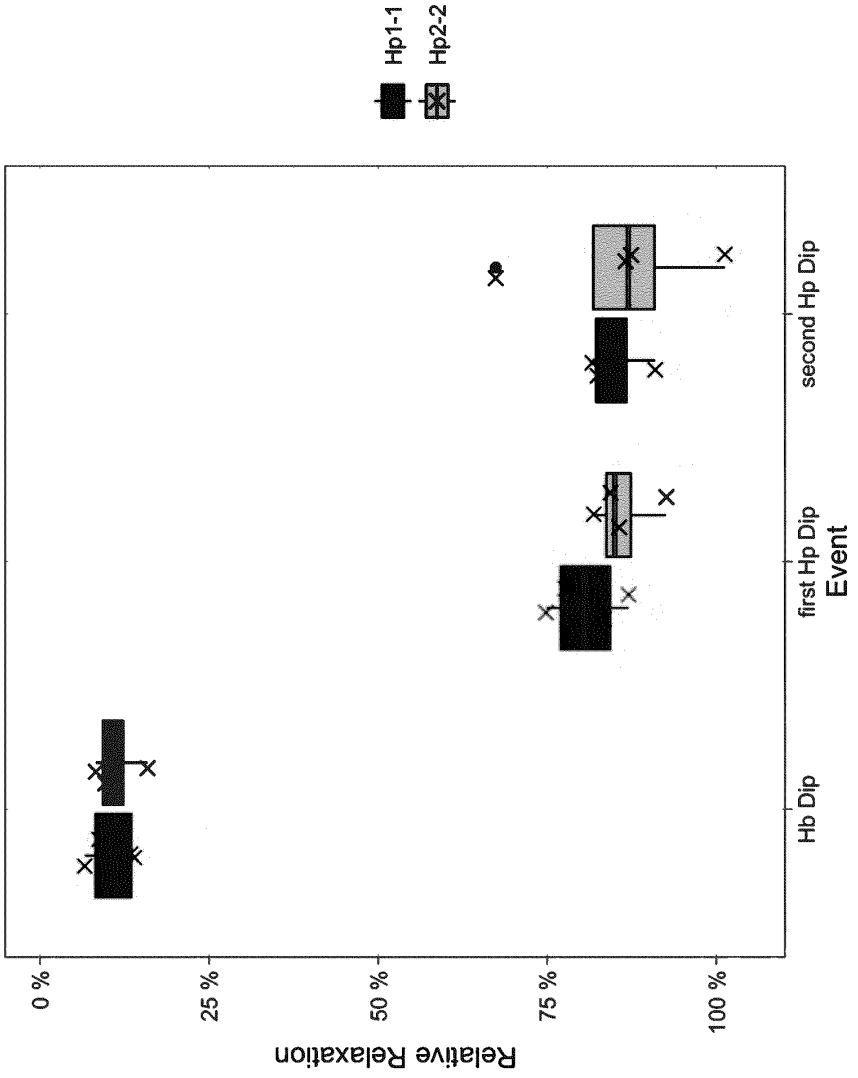

Hp1-1
Hp2-2
Relative Relaxation
0 %
25 %
50 %
75 %
100 %
Hb Dip
first Hp Dip
second Hp Dip
Event

FIGURE 18

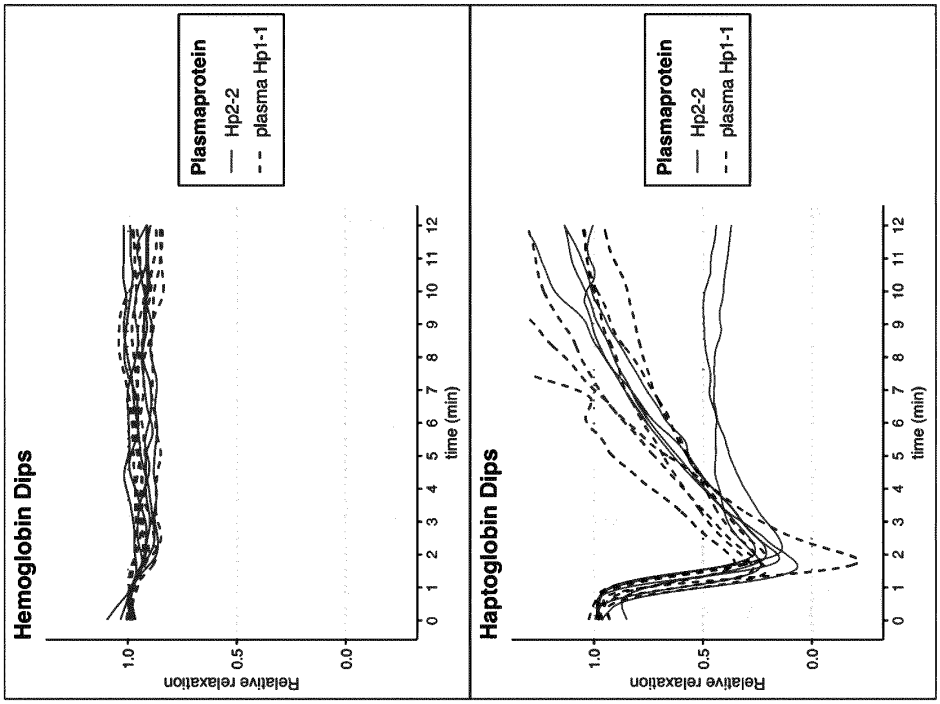

Hemoglobin Dips
Haptoglobin Dips
Plasmaprotein
Hp2-2
plasma Hp1-1
Relative relaxation
time (min)
0.0
0.5
1.0
0 1 2 3 4 5 6 7 8 9 10 11 12

FIGURE 19