Figure 1

A

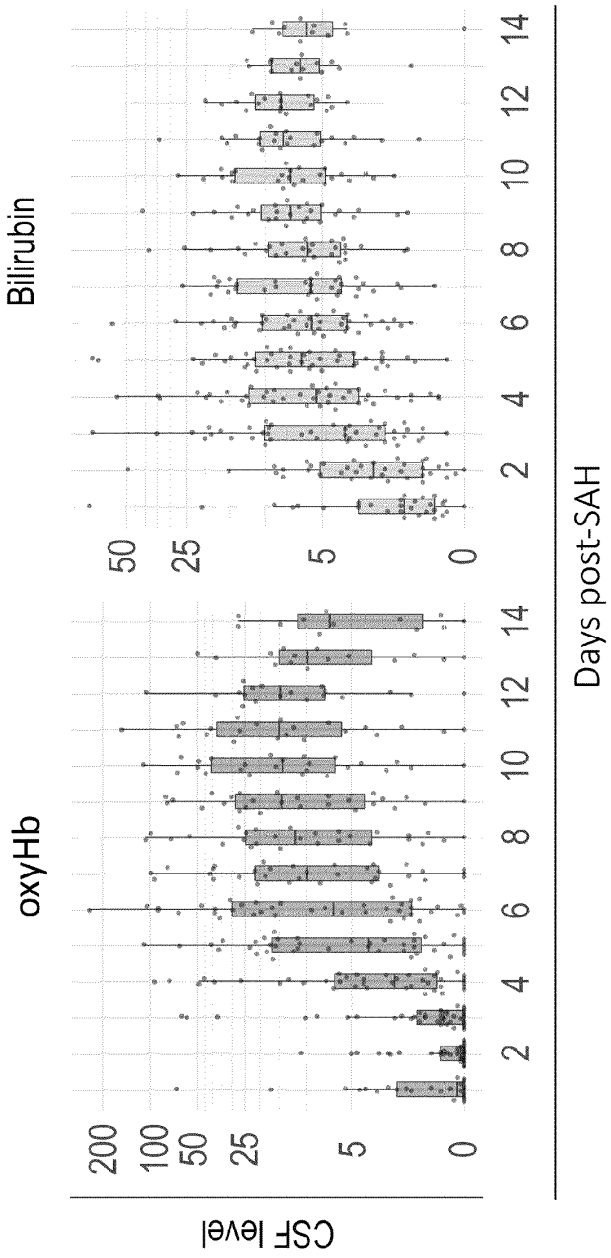

Bilirubin
oxyHb
CSF level
Days post-SAH
0
5
25
50
100
200
2
4
6
8
10
12
14

Figure 1 A (continued)

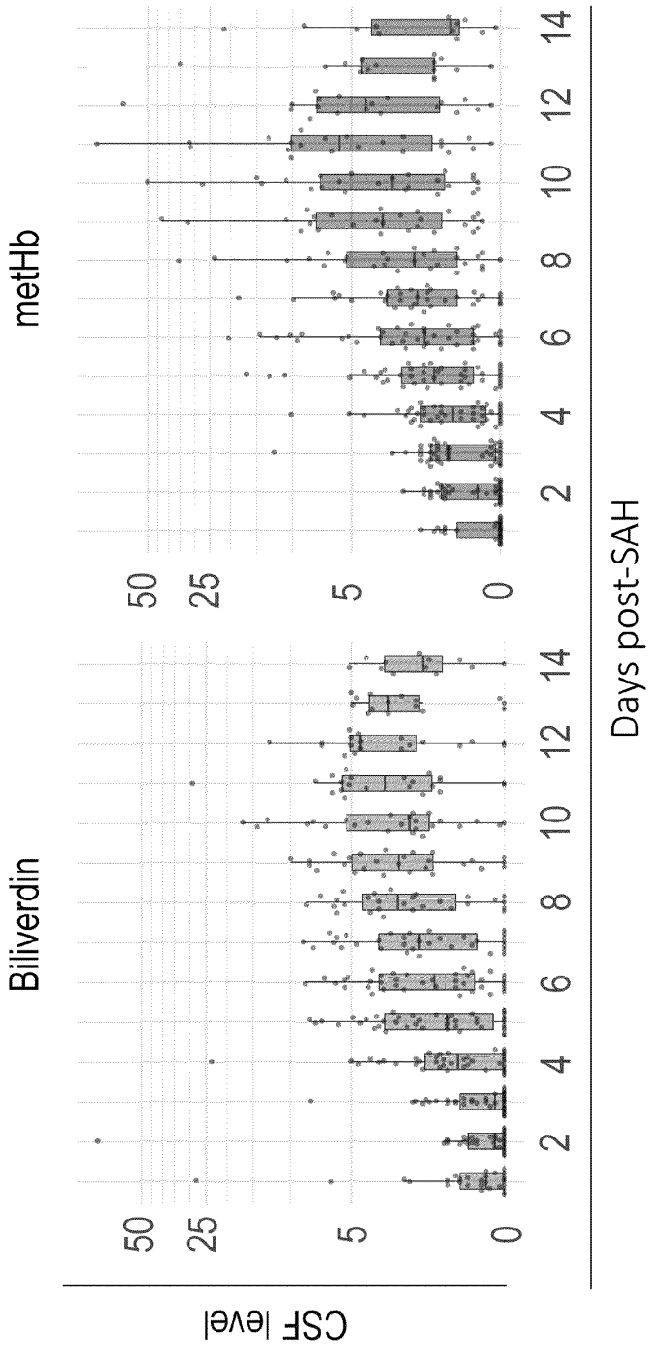


Figure 1 (continued)

B

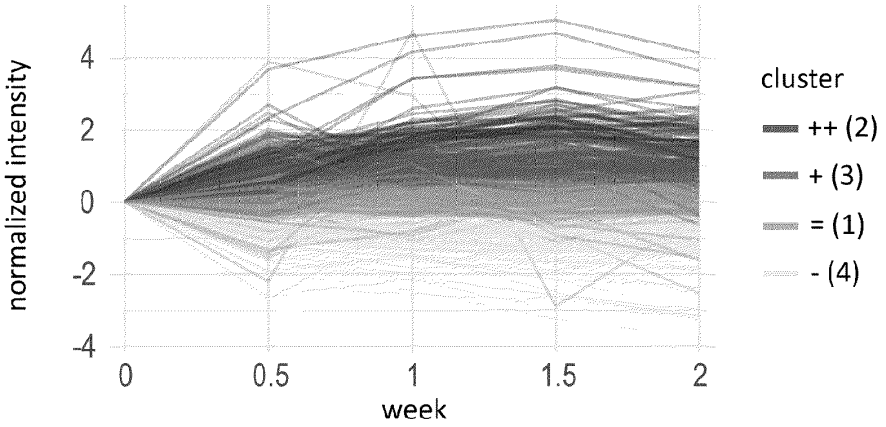


Figure 1 (continued)

C

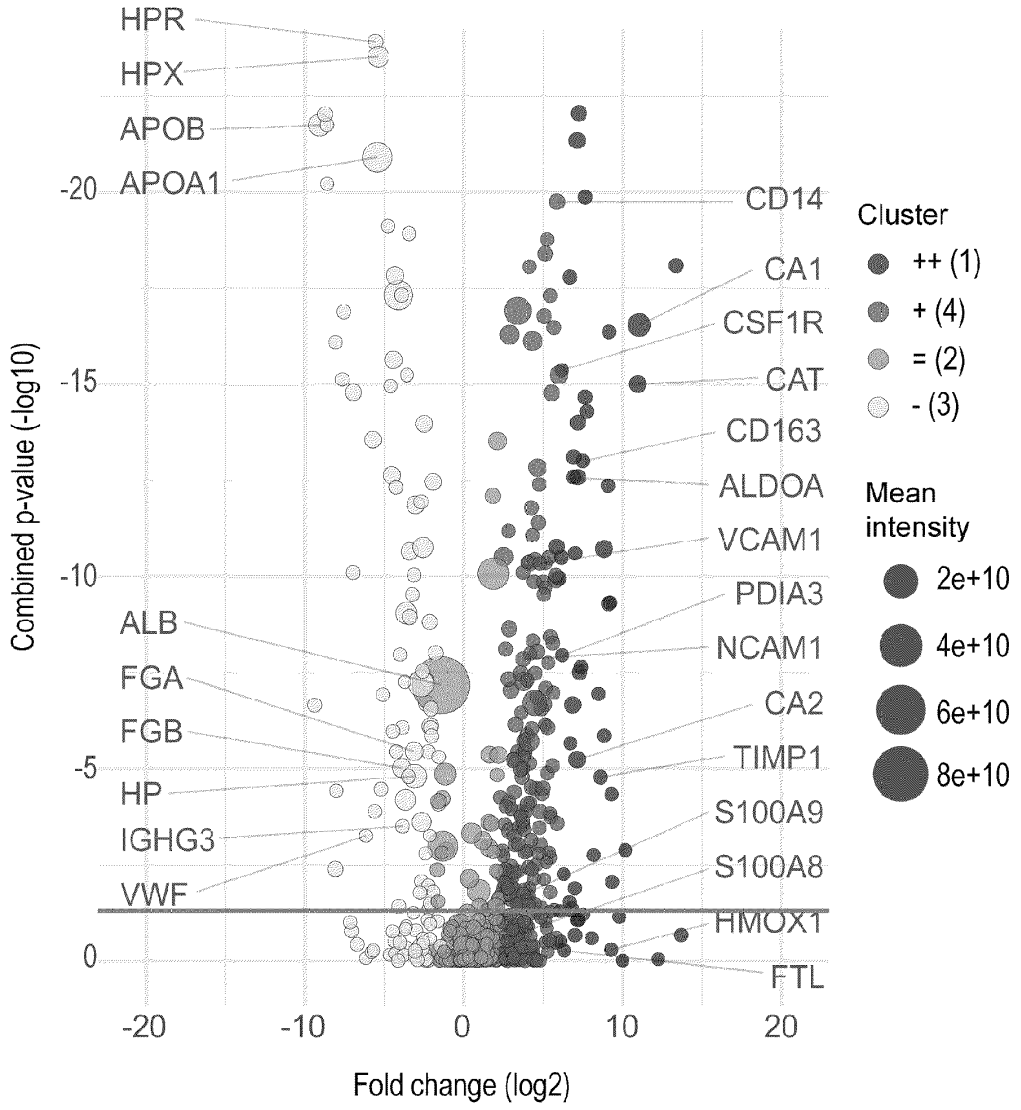


Figure 1 (continued)

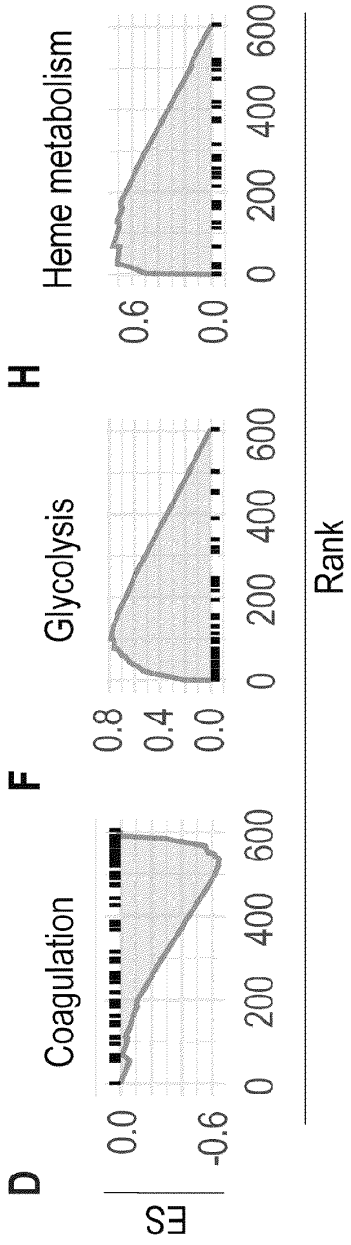


Figure 1 (continued)

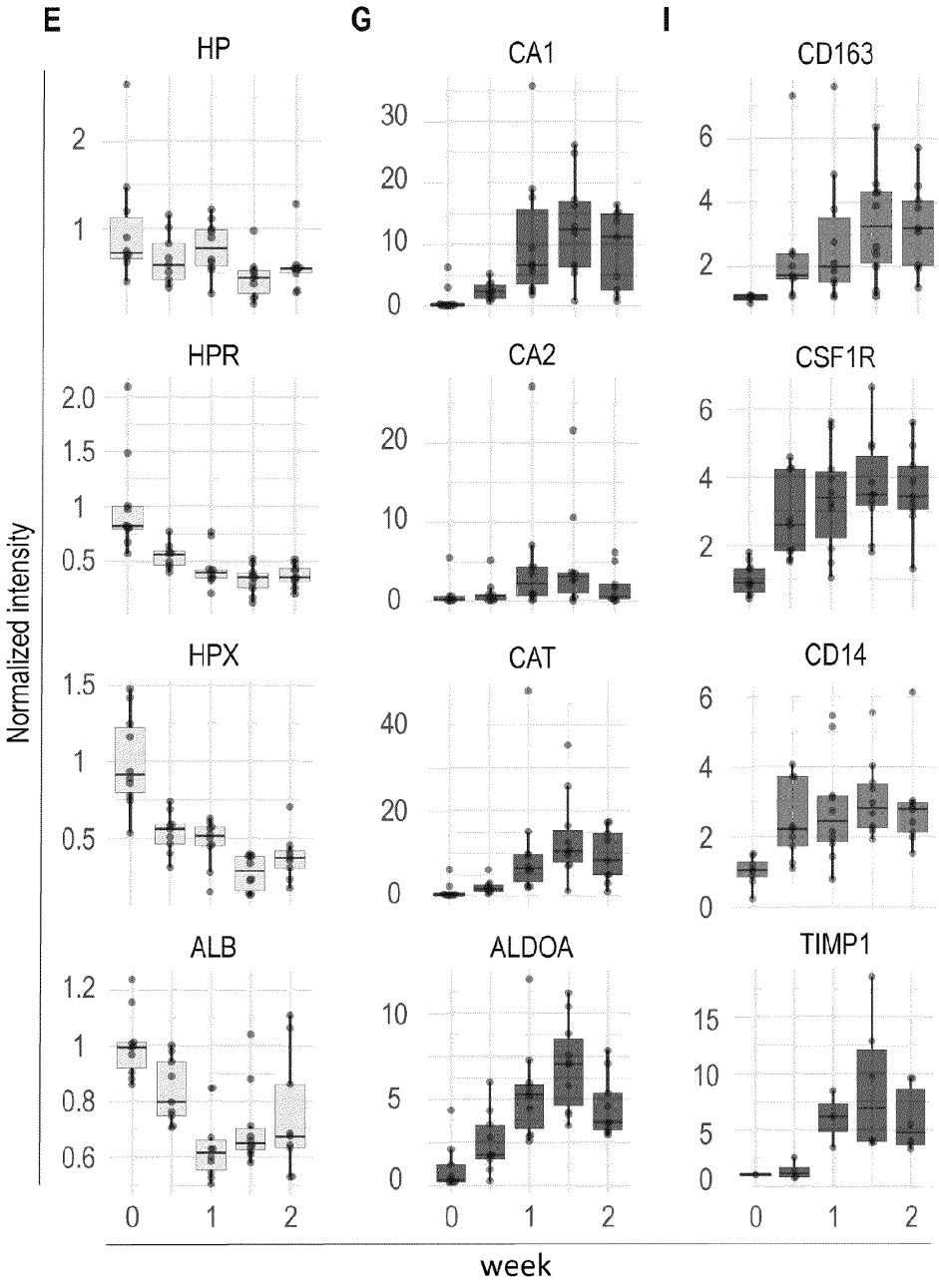


Figure 2

A



Figure 2 (continued)

B

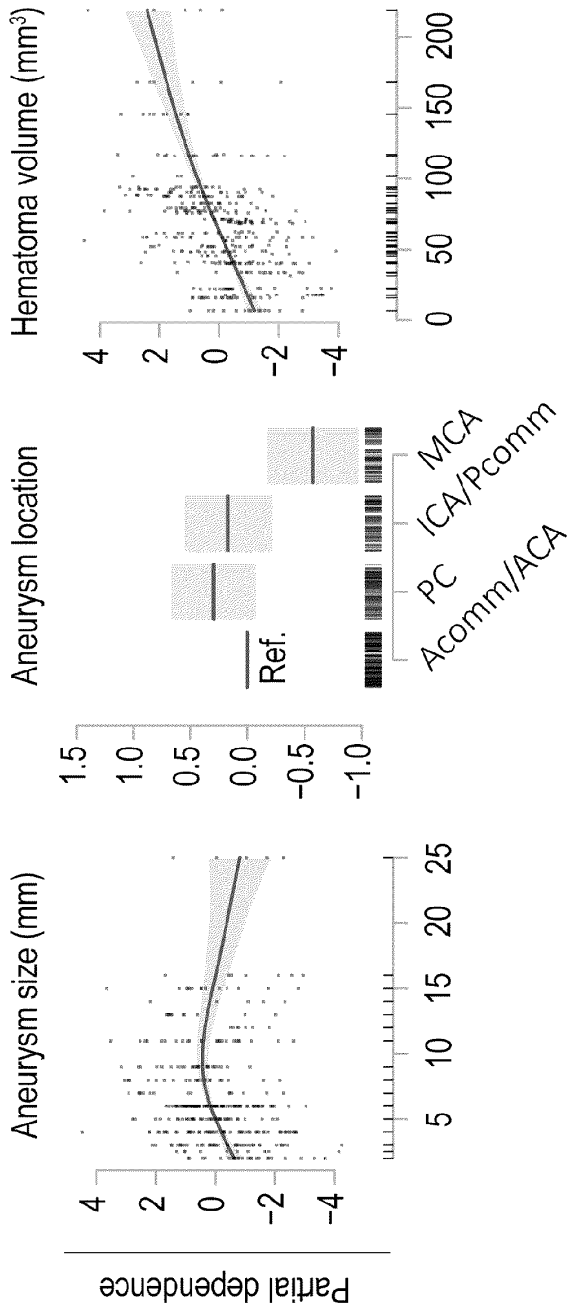


Figure 2 B (continued)

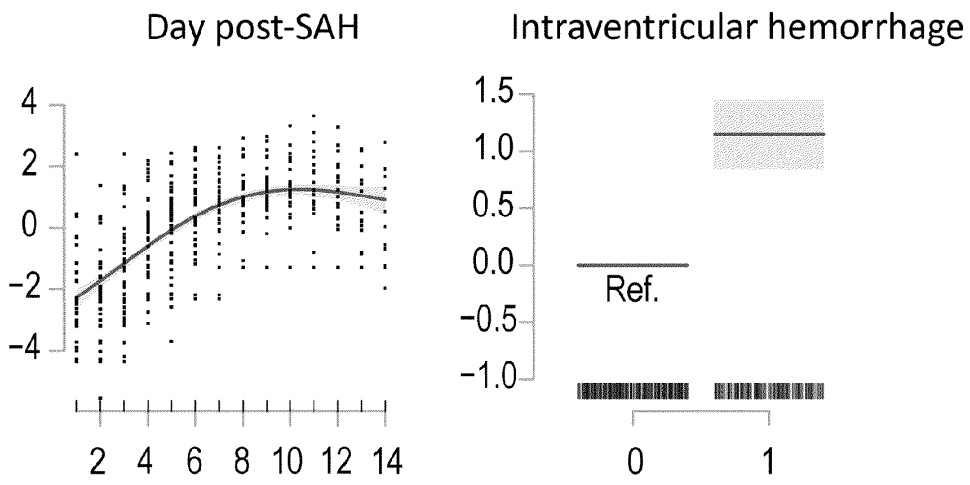


Figure 2 (continued)

C

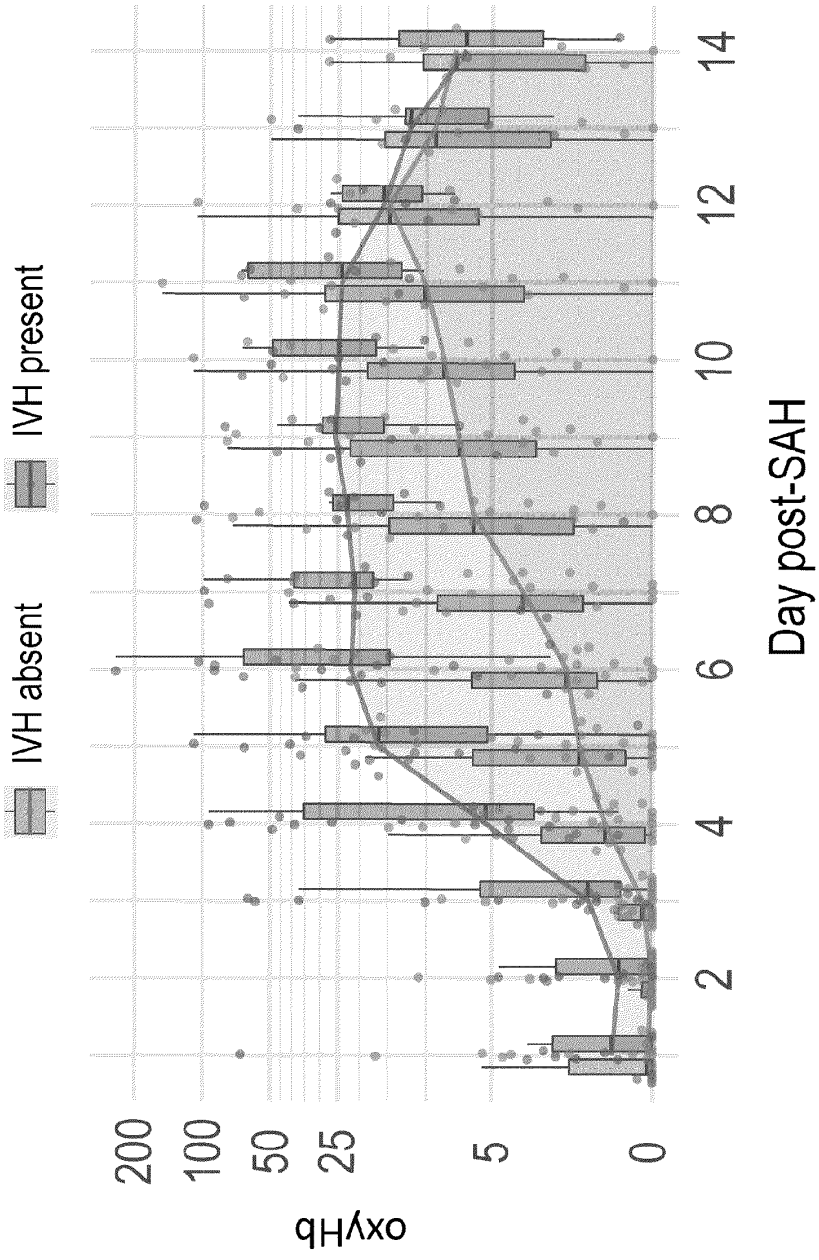


Figure 2 (continued)

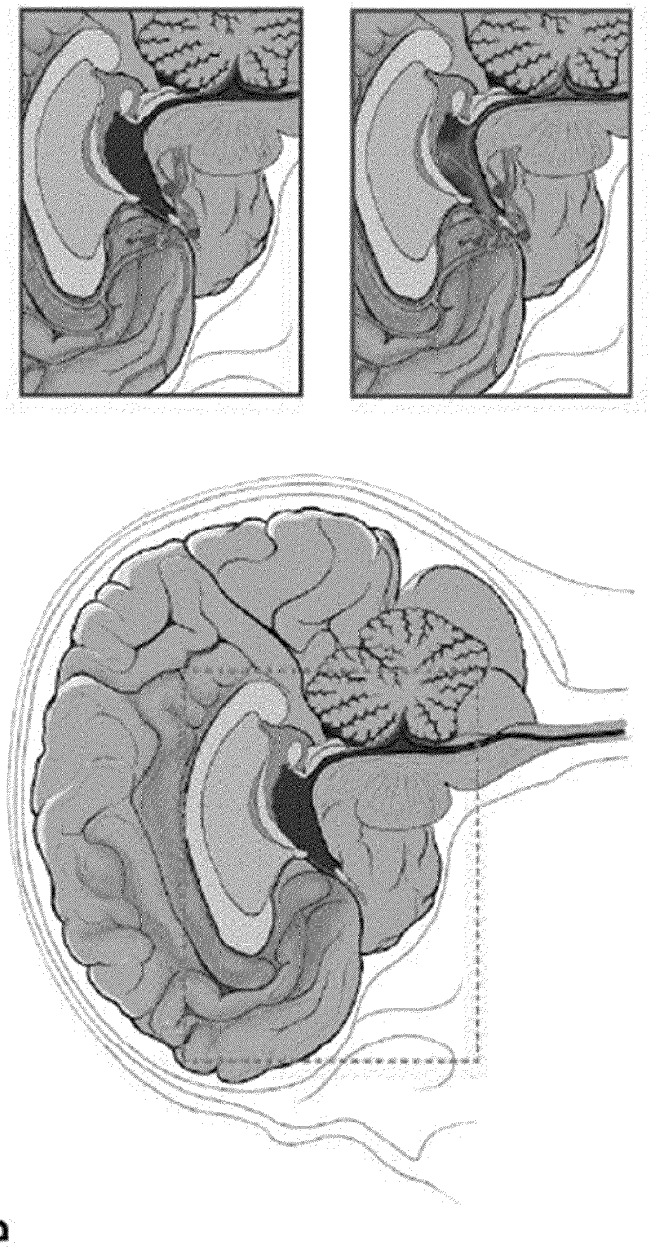


Figure 3

A

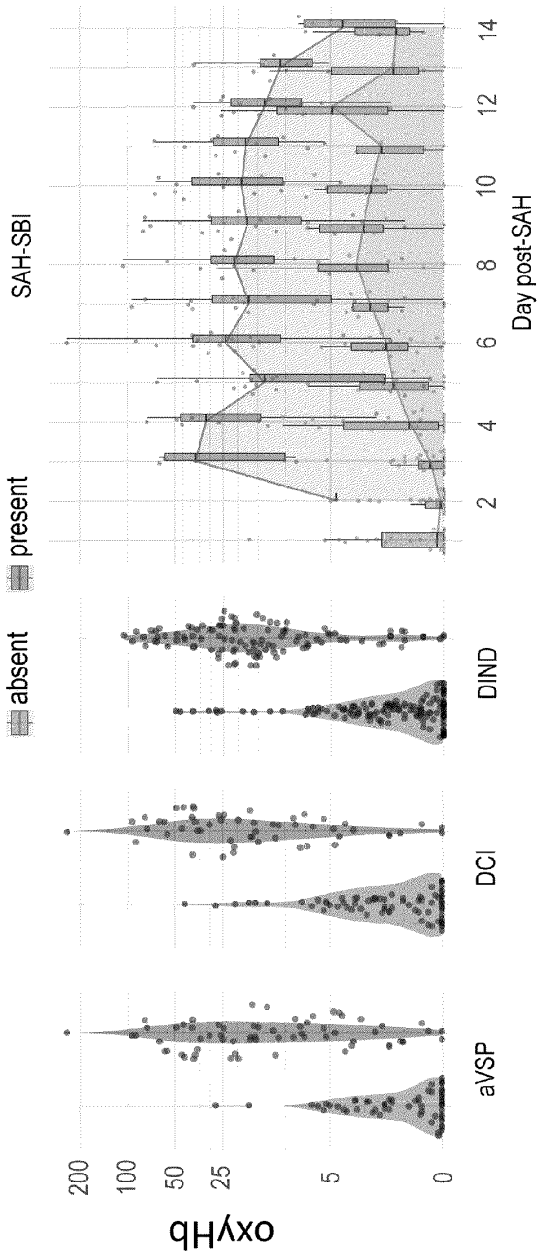

SAH-SBI
present
absent
Day post-SAH
2
4
6
8
10
12
14
DIND
DCI
aVSP
oxyHb
200
100
50
25
5
0

Figure 3 (continued)

B

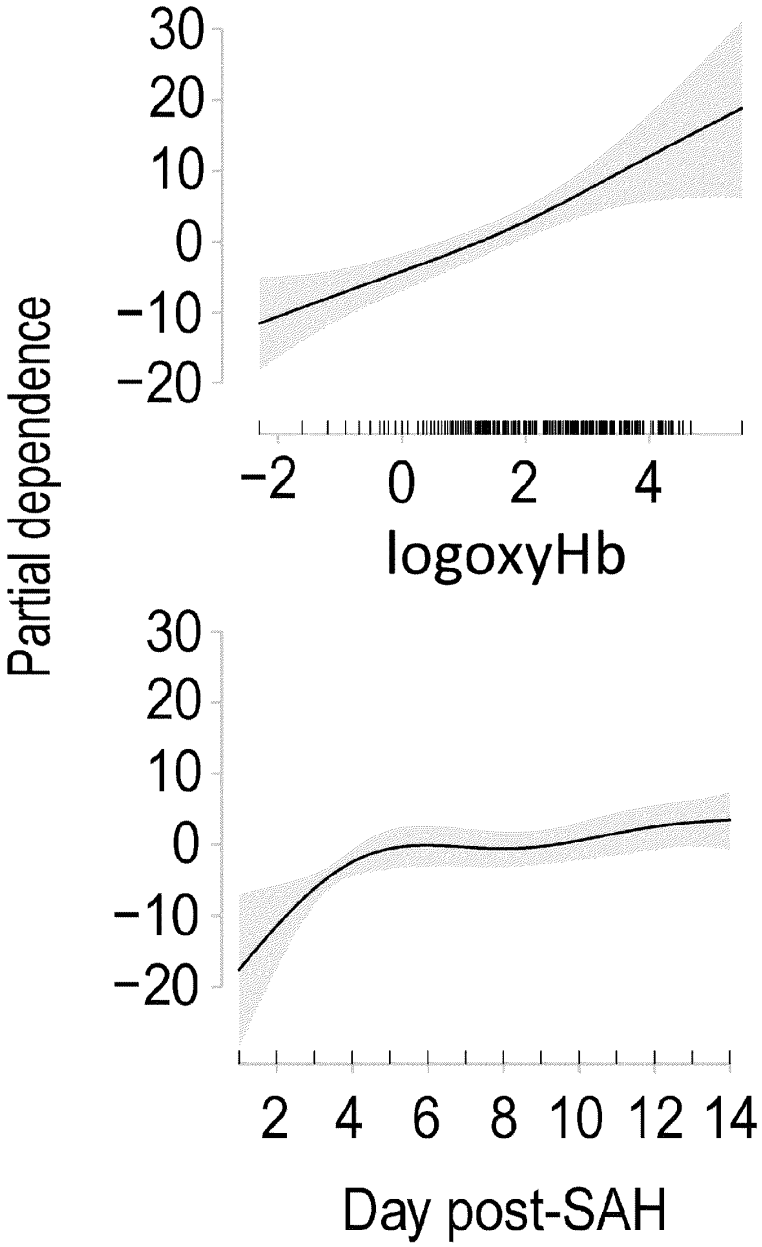


Figure 3 (continued)

C

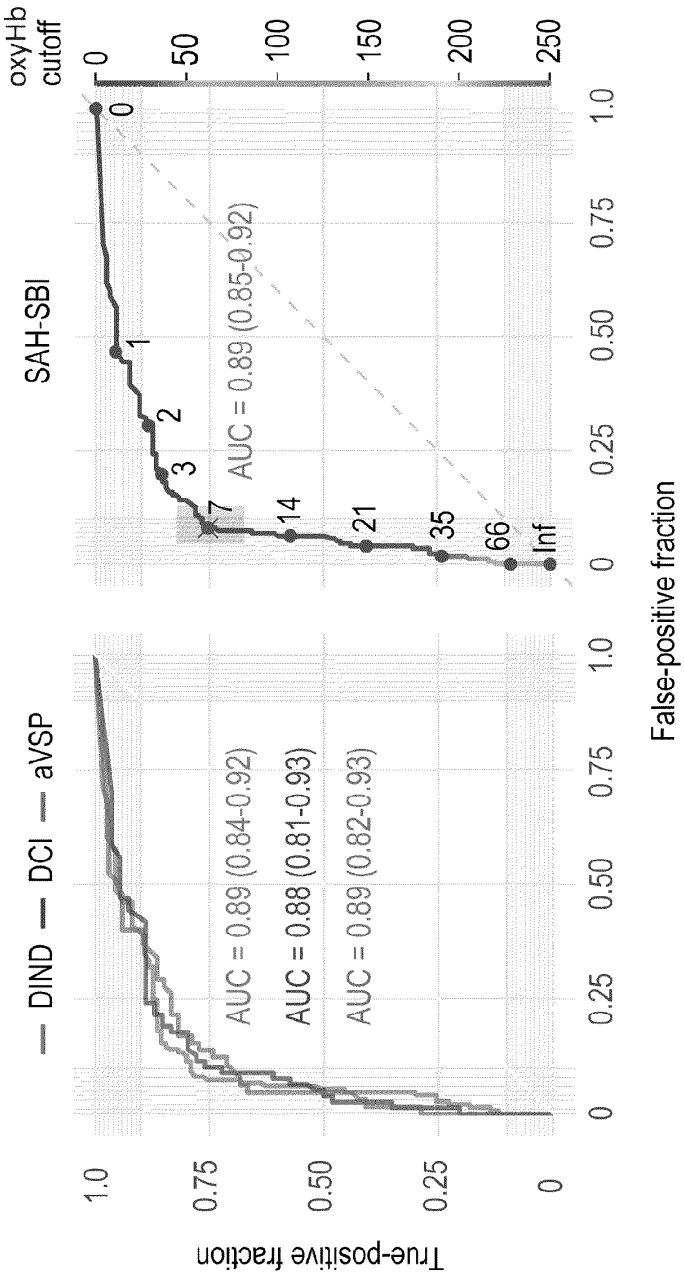


Figure 3 (continued)

D

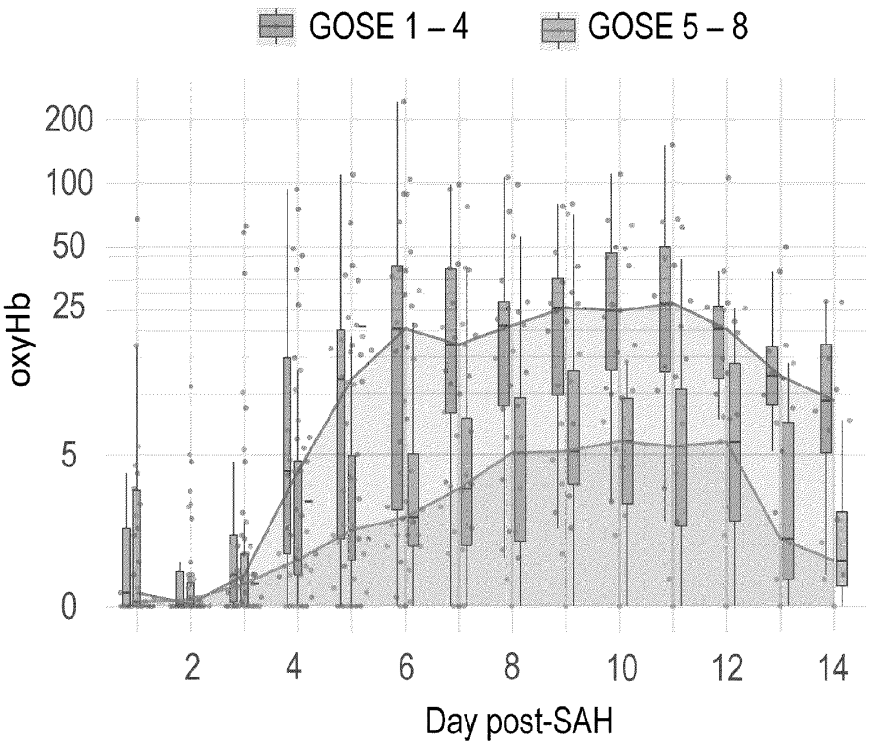


Figure 4

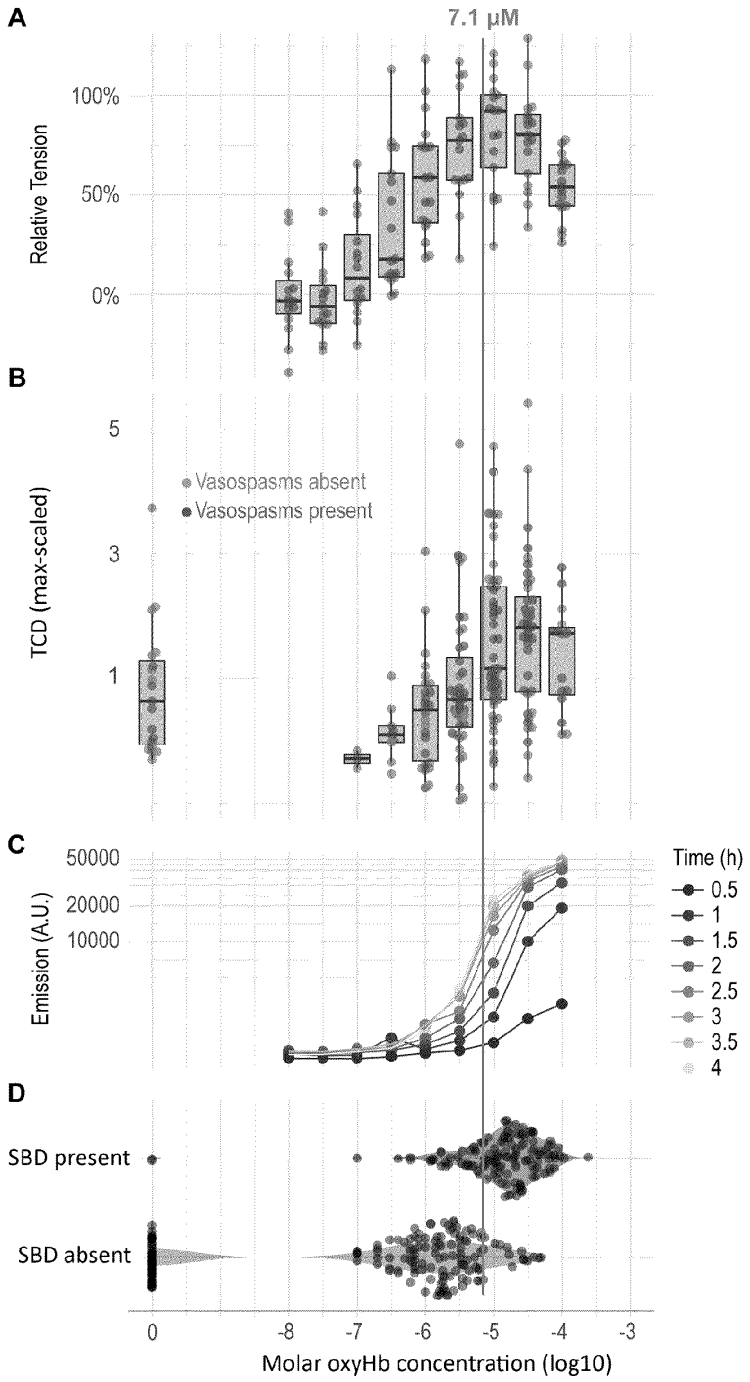

A
7.1 µM
100%
50%
0%
Relative Tension
B
5
3
1
TCD (max-scaled)
Vasospasms absent
Vasospasms present
C
50000
20000
10000
Emission (A.U.)
Time (h)
0.5
1
1.5
2
2.5
3
3.5
4
D
SBD present
SBD absent
0
-8
-7
-6
-5
-4
-3
Molar oxyHb concentration (log10)

Figure 5

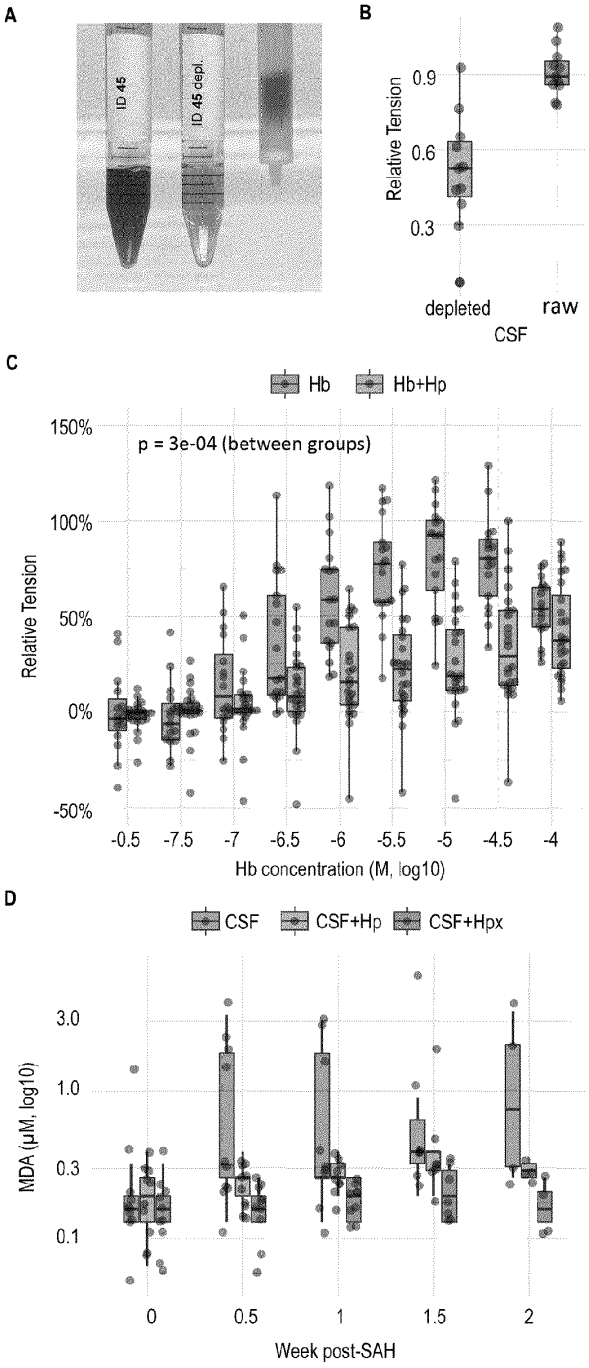
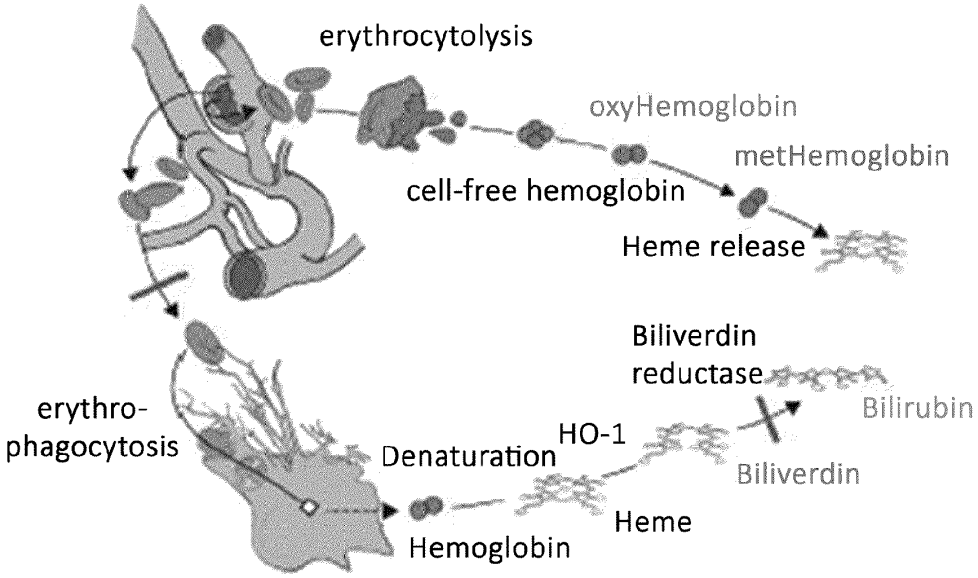

A
ID 45
ID 45 depl.
B
Relative Tension
0.9
0.6
0.3
depleted
raw
CSF
C
Hb
Hb+Hp
p = 3e-04 (between groups)
150%
100%
50%
0%
-50%
Relative Tension
-0.5
-7.5
-7
-6.5
-6
-5.5
-5
-4.5
-4
Hb concentration (M, log10)
D
CSF
CSF+Hp
CSF+Hpx
3.0
1.0
0.3
0.1
MDA (µM, log10)
0
0.5
1
1.5
2
Week post-SAH

Figure 6

A


erythrocytolysis
oxyHemoglobin
metHemoglobin
cell-free hemoglobin
Heme release
Biliverdin
reductase
Bilirubin
erythro-
phagocytosis
HO-1
Denaturation
Biliverdin
Heme
Hemoglobin

B

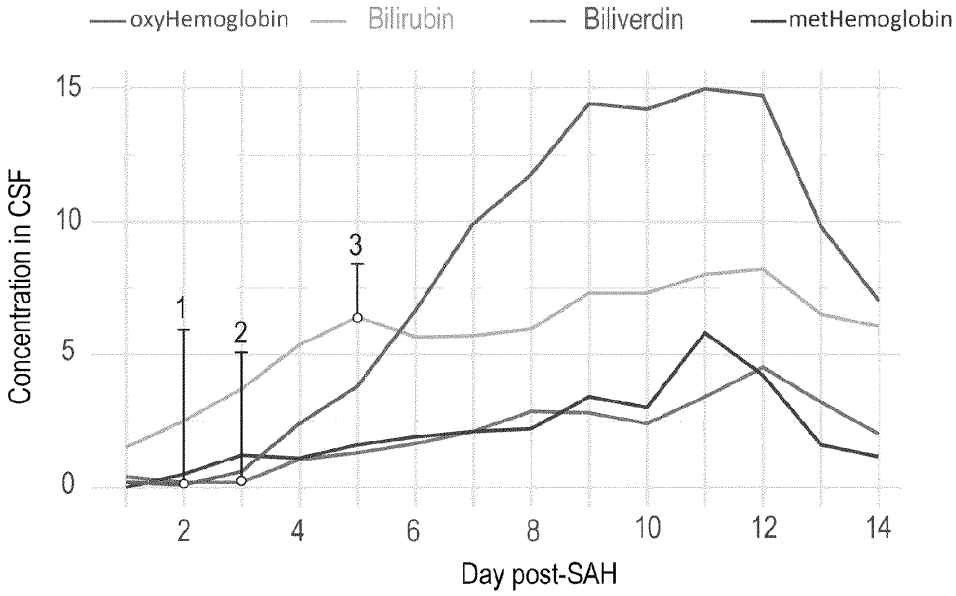

oxyHemoglobin
Bilirubin
Biliverdin
metHemoglobin
Concentration in CSF
15
10
5
0
1
2
3
2
4
6
8
10
12
14
Day post-SAH

Figure 7

A

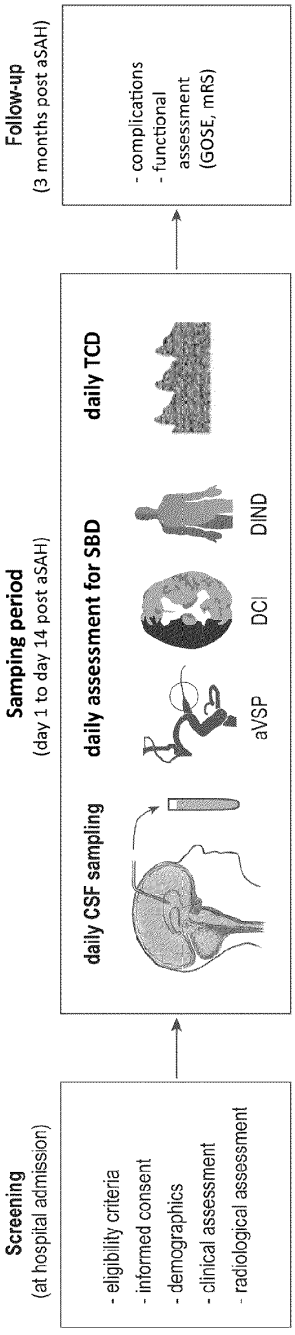

Screening
(at hospital admission)
- eligibility criteria
- informed consent
- demographics
- clinical assessment
- radiological assessment
Samping period
(day 1 to day 14 post aSAH)
daily CSF sampling
daily assessment for SBD
aVSP
DCI
DIND
daily TCD
Follow-up
(3 months post aSAH)
- complications
- functional assessment
(GOSE, mRS)

Figure 7 (continued)

B

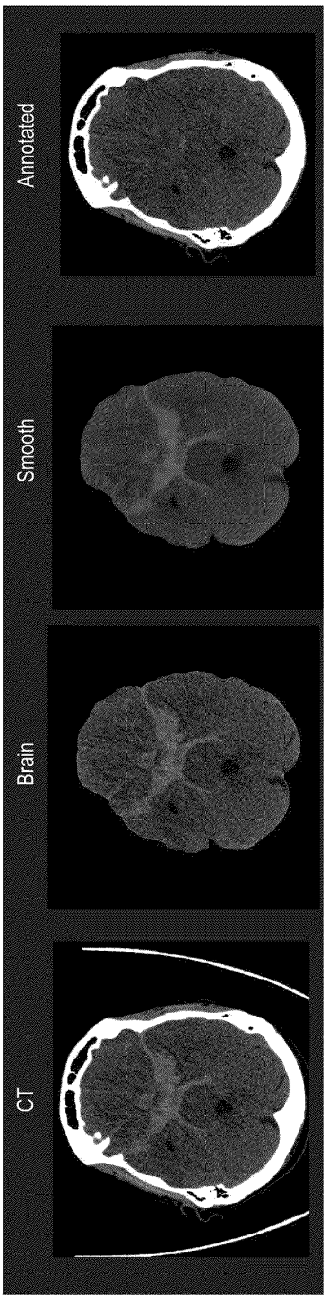


Figure 7 (continued)

C

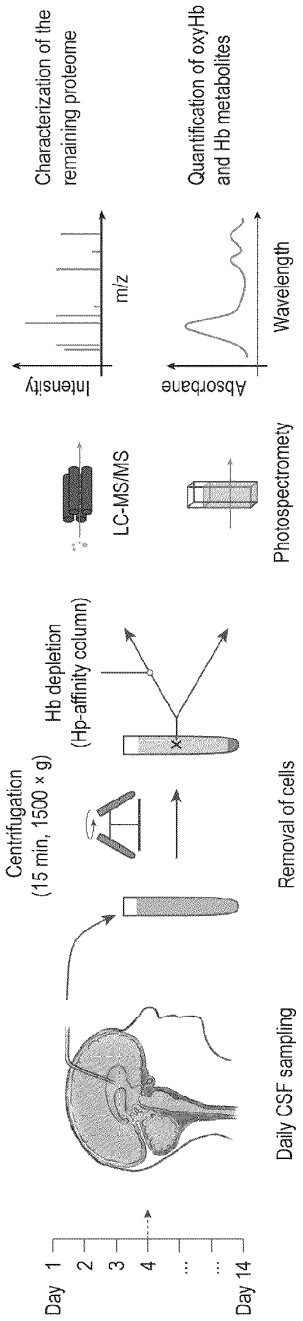
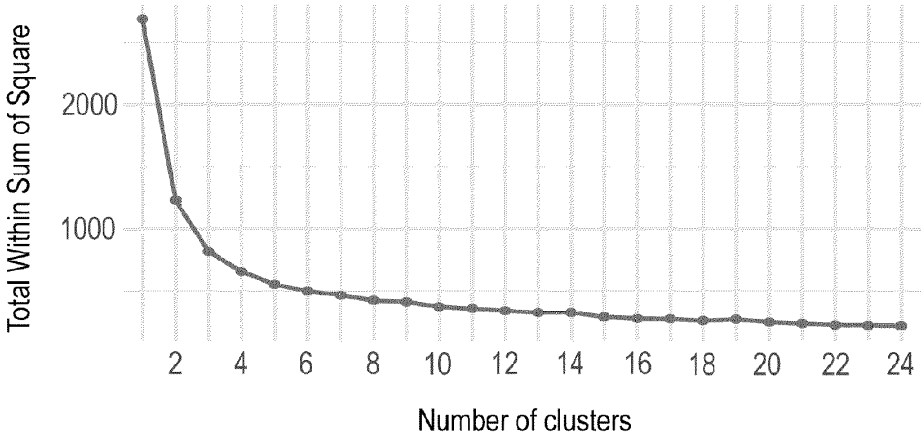


Figure 7 (continued)

D



E

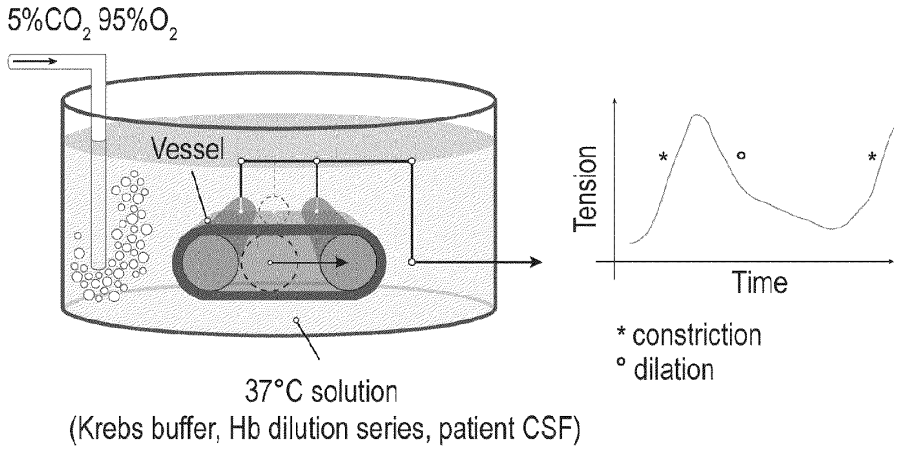
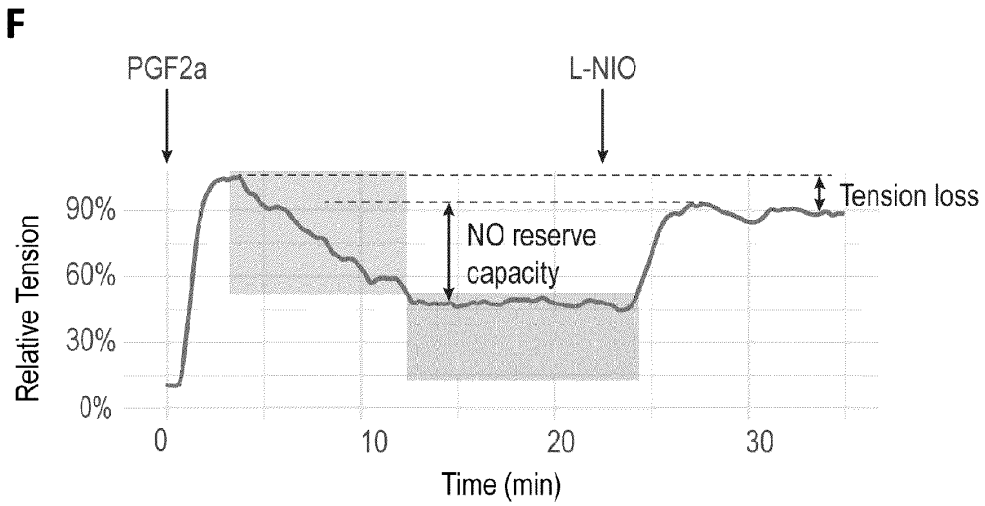


Figure 7 (continued)



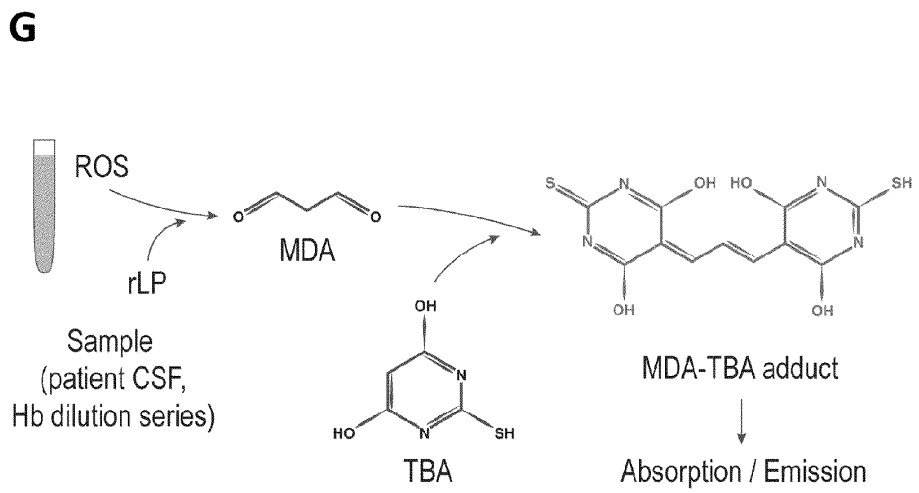


Figure 8

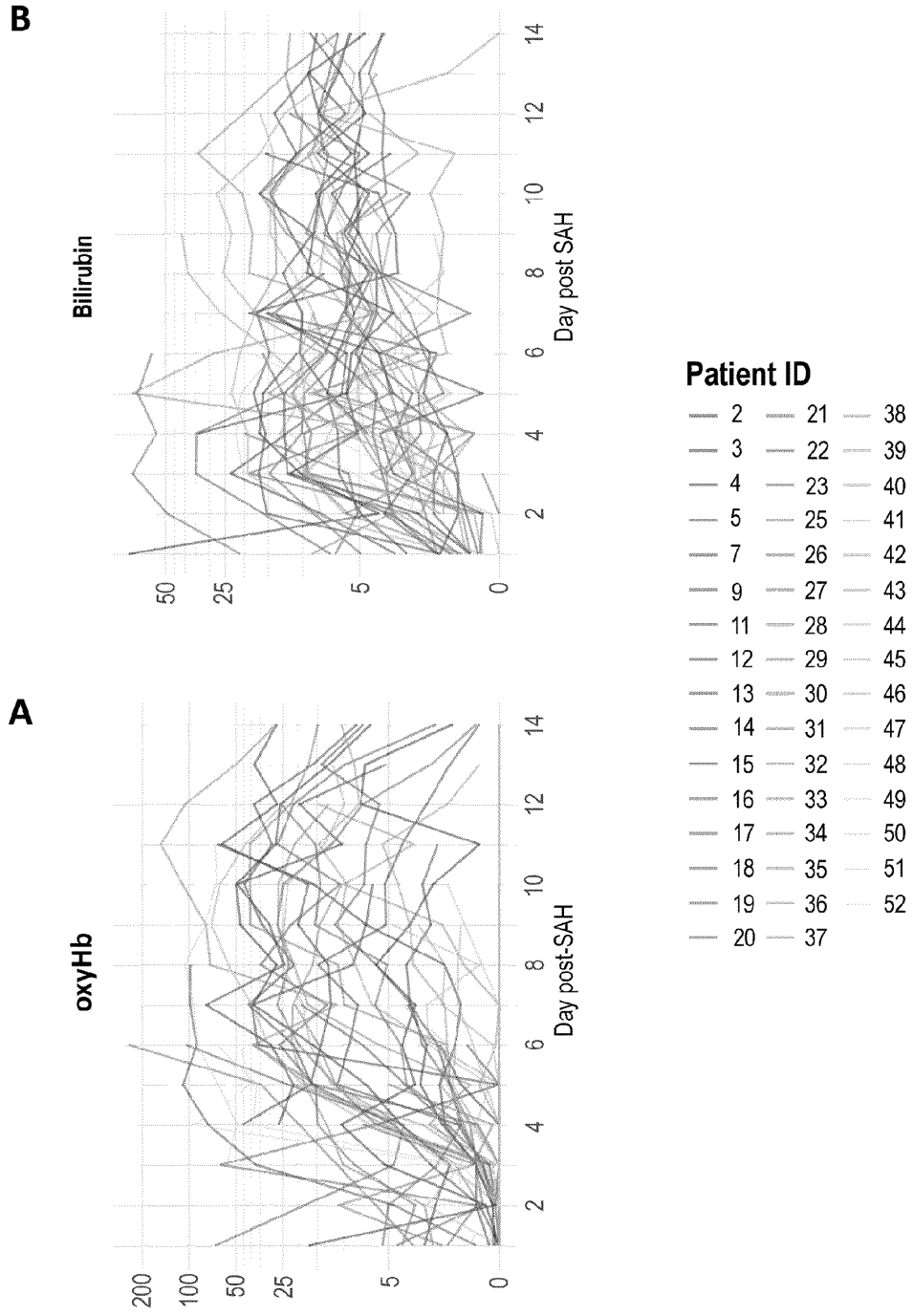

B
Bilirubin
50
25
5
0
2
4
6
8
10
12
14
Day post SAH
A
oxyHb
200
100
50
25
5
0
2
4
6
8
10
12
14
Day post-SAH
Patient ID
2 21 38
3 22 39
4 23 40
5 25 41
7 26 42
9 27 43
11 28 44
12 29 45
13 30 46
14 31 47
15 32 48
16 33 49
17 34 50
18 35 51
19 36 52
20 37

Figure 8 (continued)

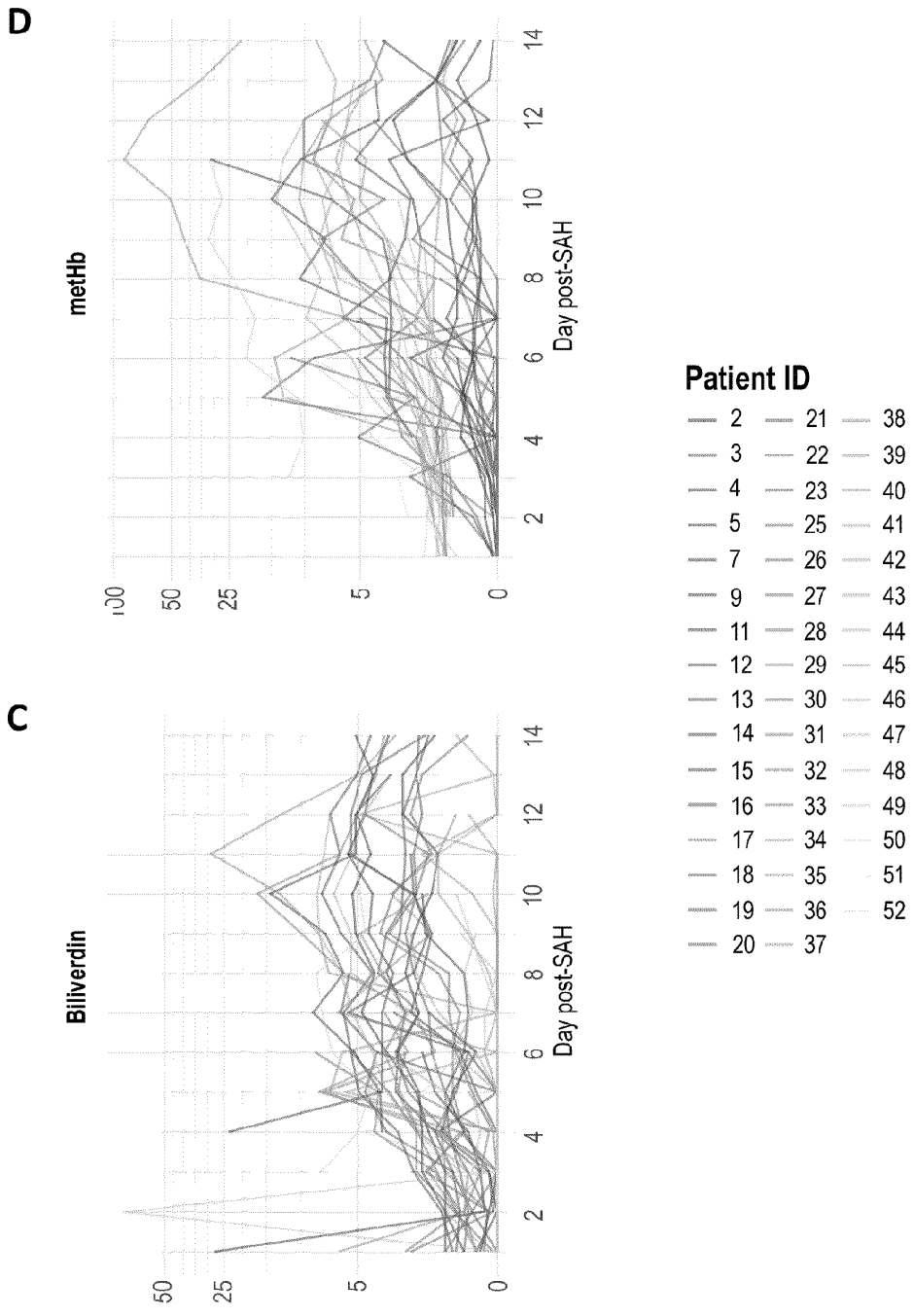


Figure 9

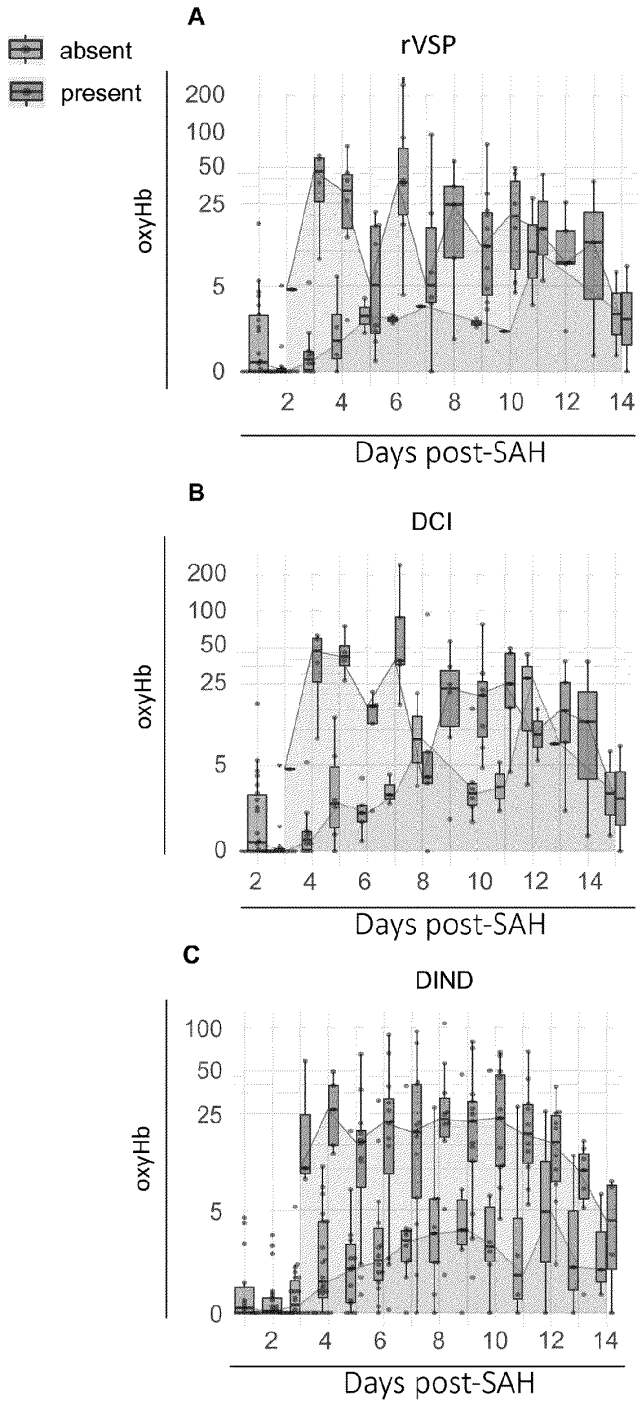

A
absent
present
rVSP
oxyHb
200
100
50
25
5
0
2 4 6 8 10 12 14
Days post-SAH
B
DCI
oxyHb
200
100
50
25
5
0
2 4 6 8 10 12 14
Days post-SAH
C
DIND
oxyHb
100
50
25
5
0
2 4 6 8 10 12 14
Days post-SAH

Figure 10

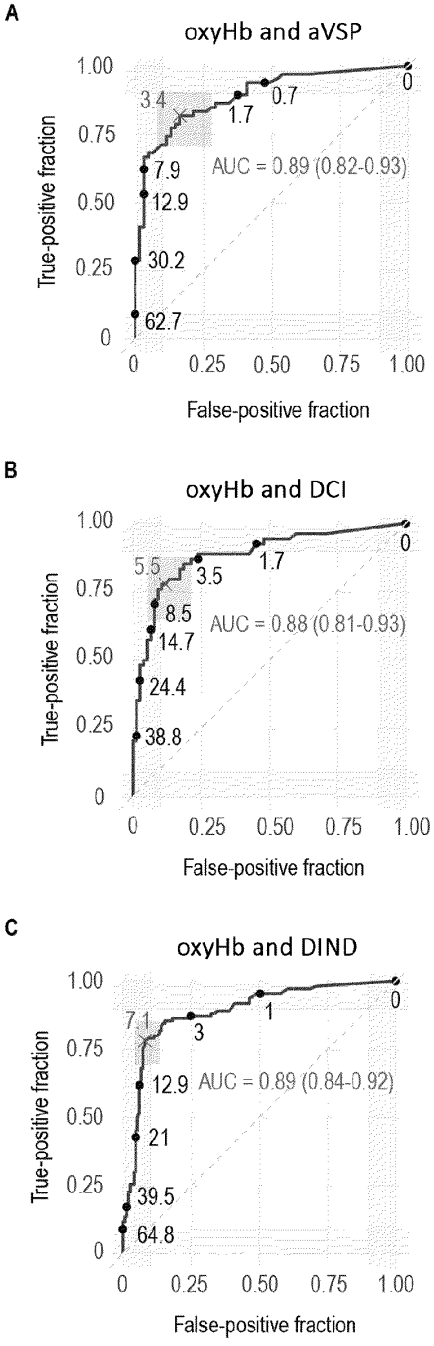

A
oxyHb and aVSP
True-positive fraction
False-positive fraction
AUC = 0.89 (0.82-0.93)
3.4
1.7
0.7
0
7.9
12.9
30.2
62.7
B
oxyHb and DCI
True-positive fraction
False-positive fraction
AUC = 0.88 (0.81-0.93)
5.5
3.5
1.7
0
8.5
14.7
24.4
38.8
C
oxyHb and DIND
True-positive fraction
False-positive fraction
AUC = 0.89 (0.84-0.92)
7.1
3
1
0
12.9
21
39.5
64.8

Figure 10 (continued)

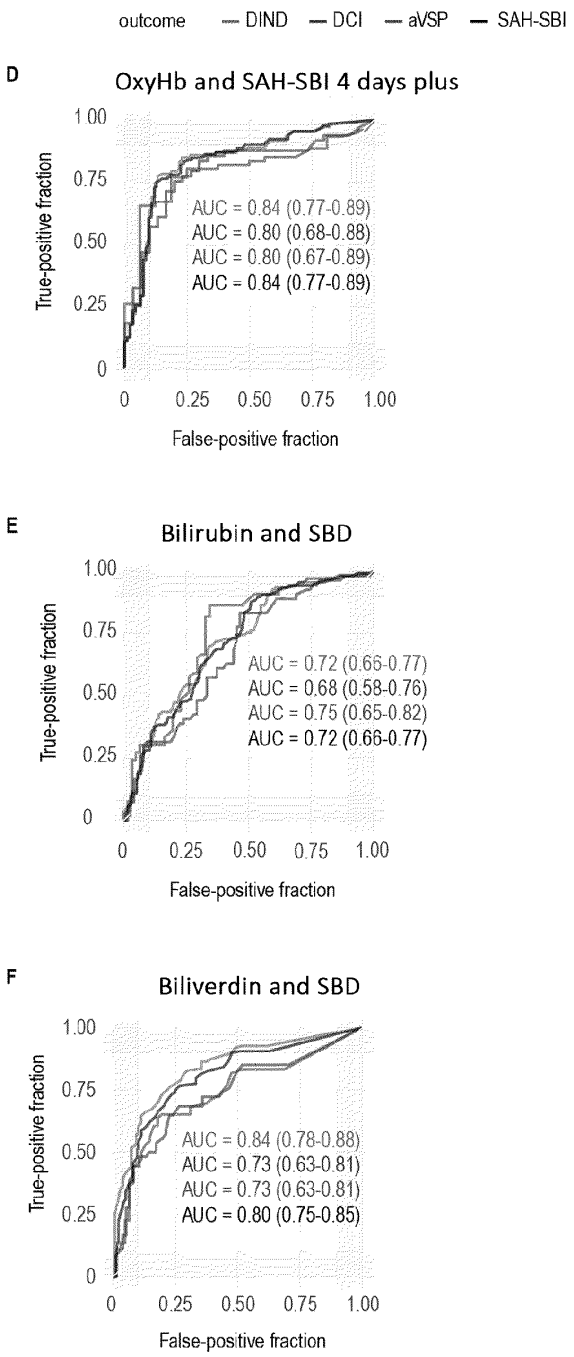


Figure 10 (continued)

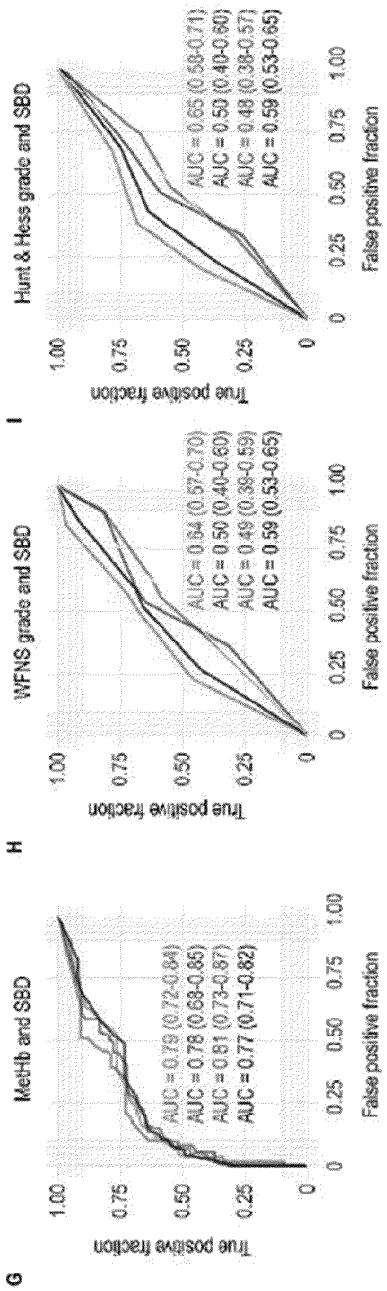


Figure 10 (continued)

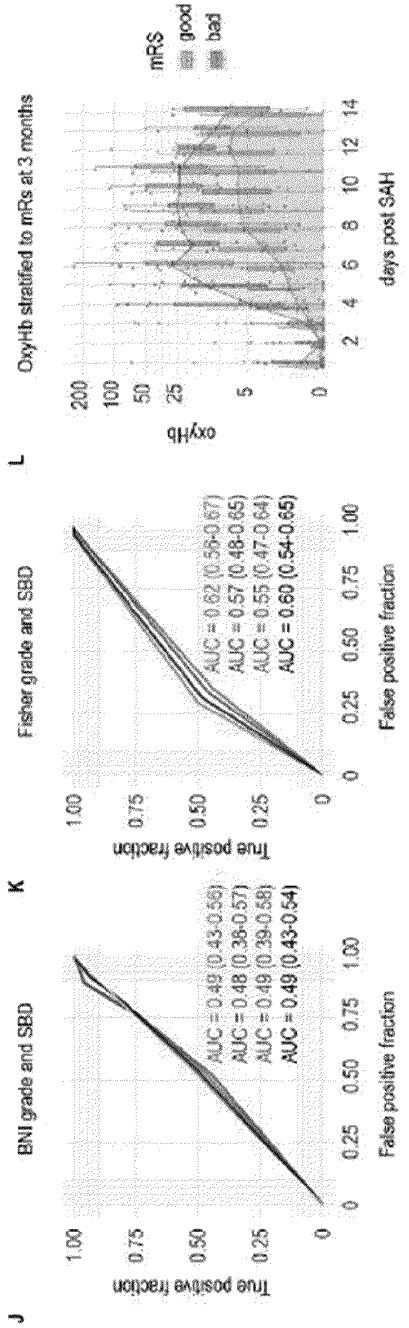


Figure 11

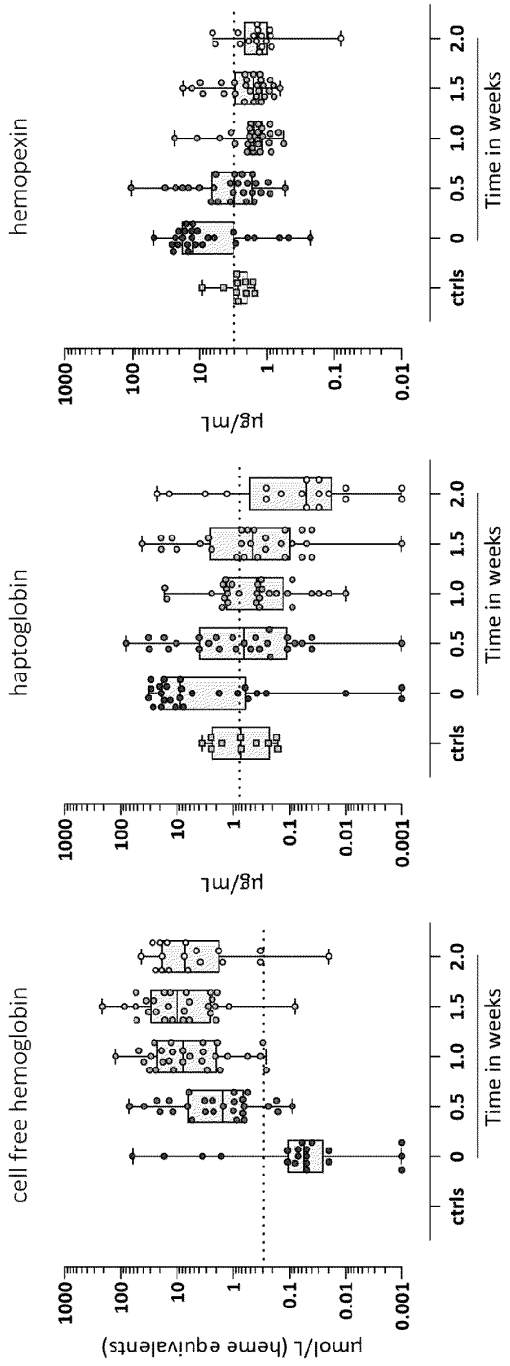

cell free hemoglobin
μmol/L (heme equivalents)
1000
100
10
1
0.1
0.01
0.001
ctrls
0
0.5
1.0
1.5
2.0
Time in weeks
haptoglobin
μg/mL
1000
100
10
1
0.1
0.01
0.001
ctrls
0
0.5
1.0
1.5
2.0
Time in weeks
hemopexin
μg/mL
1000
100
10
1
0.1
0.01
ctrls
0
0.5
1.0
1.5
2.0
Time in weeks

Figure 11 (continued)

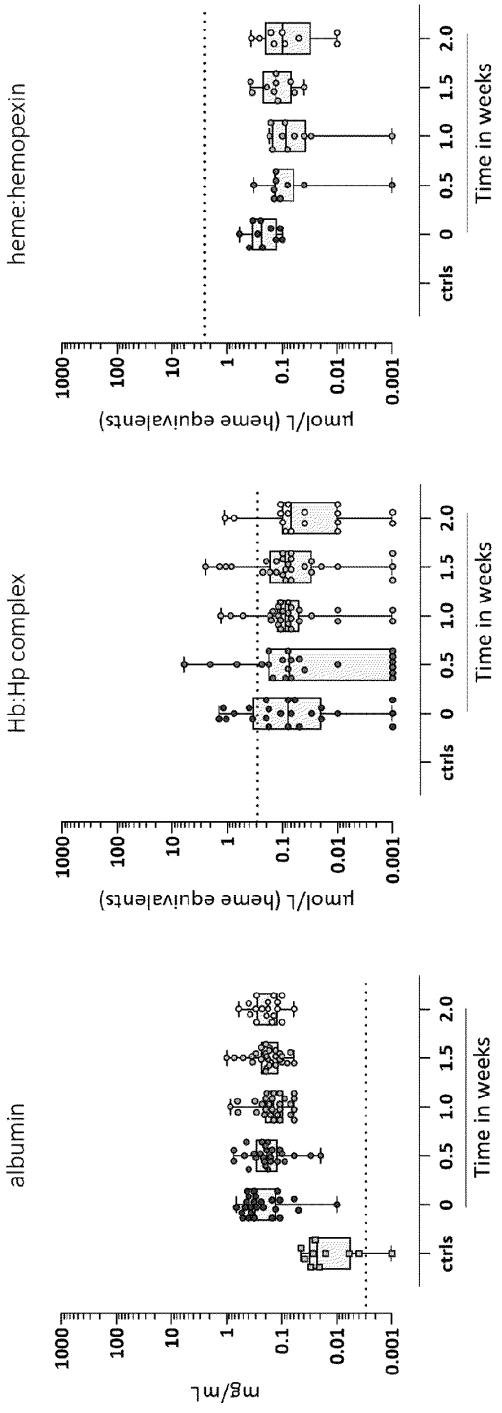


Figure 11 (continued)

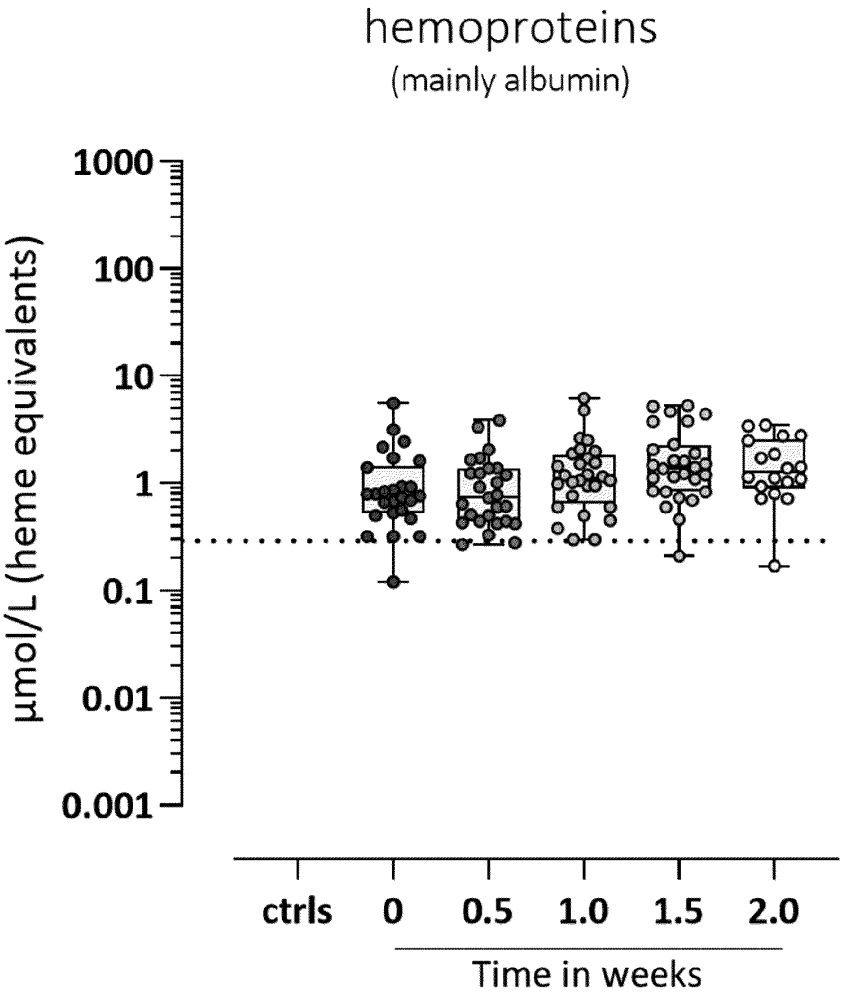


Figure 12

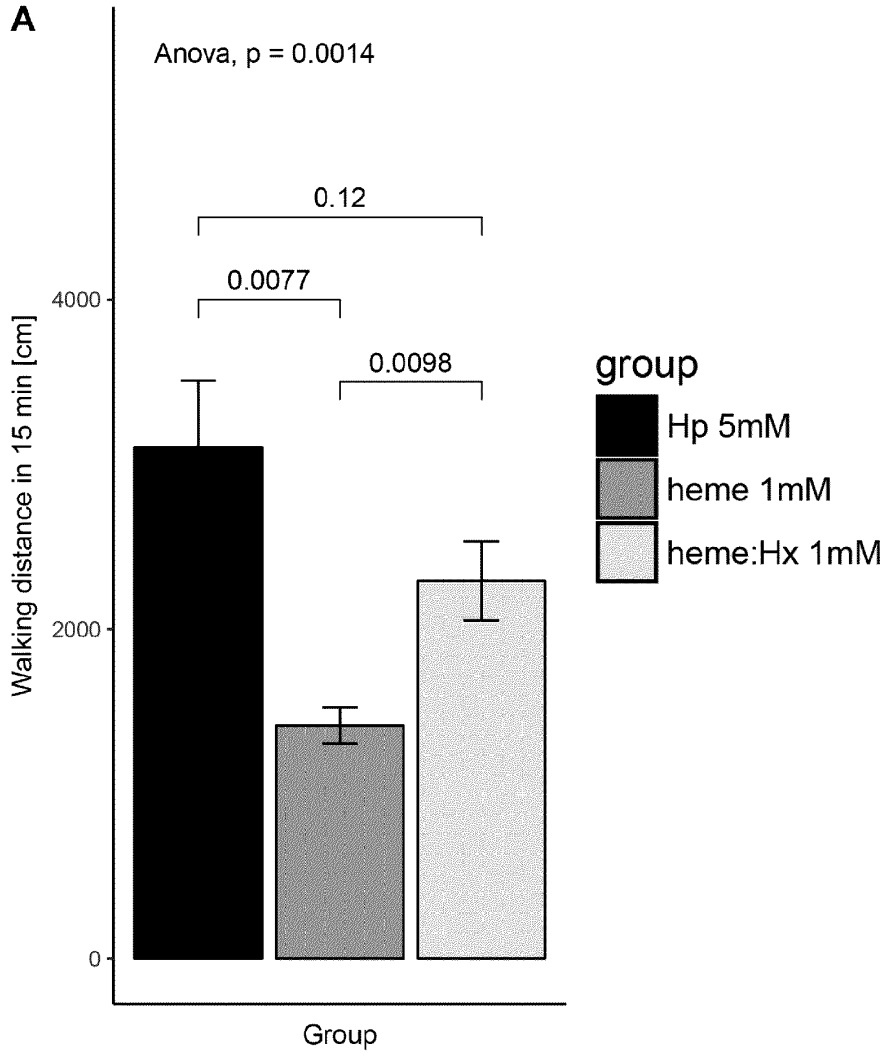

A
Anova, p = 0.0014
0.12
0.0077
0.0098
4000
2000
0
Walking distance in 15 min [cm]
Group
group
Hp 5mM
heme 1mM
heme:Hx 1mM

Figure 12 (continued)

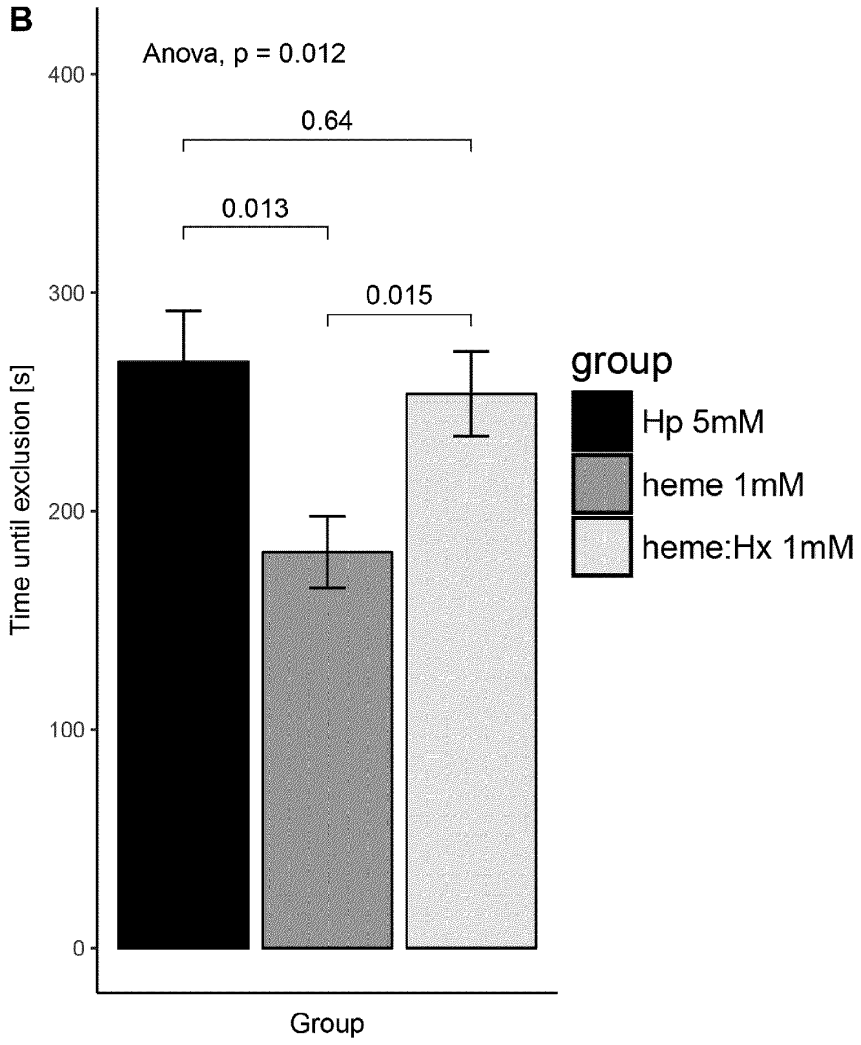


Figure 12 (continued)

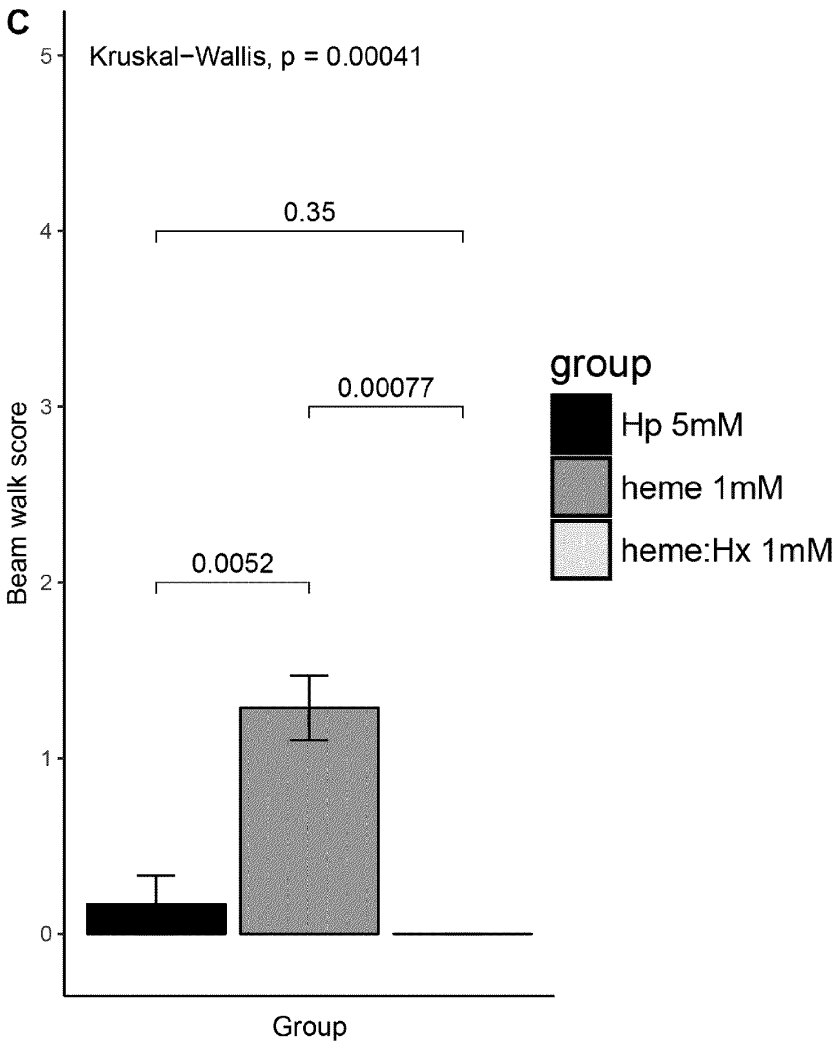


Figure 13

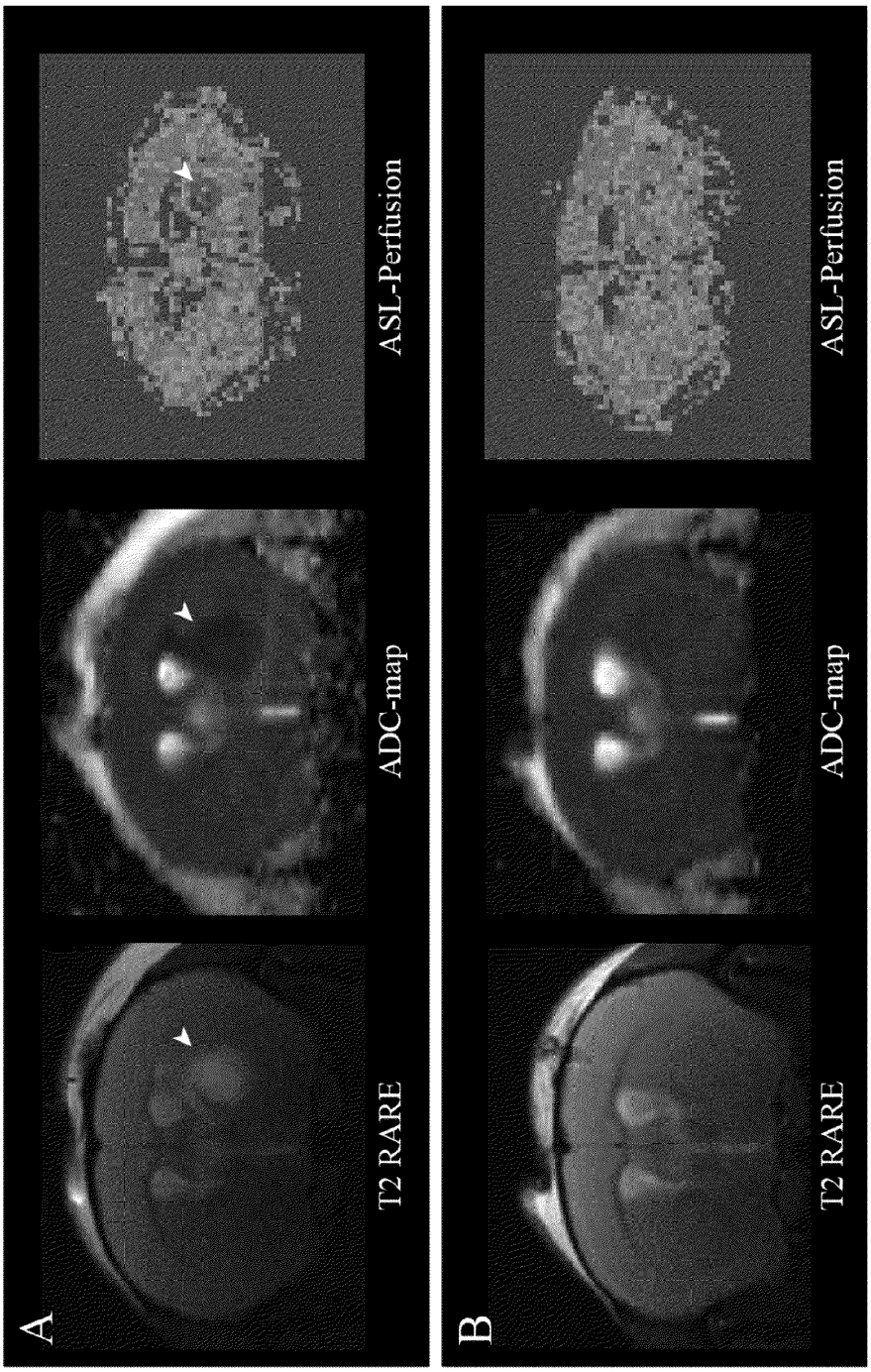
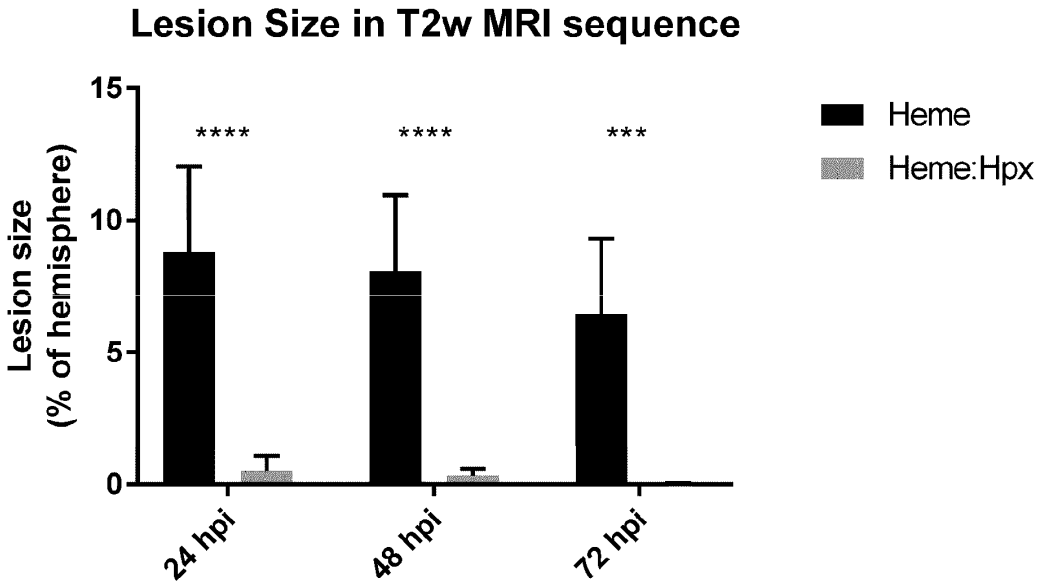
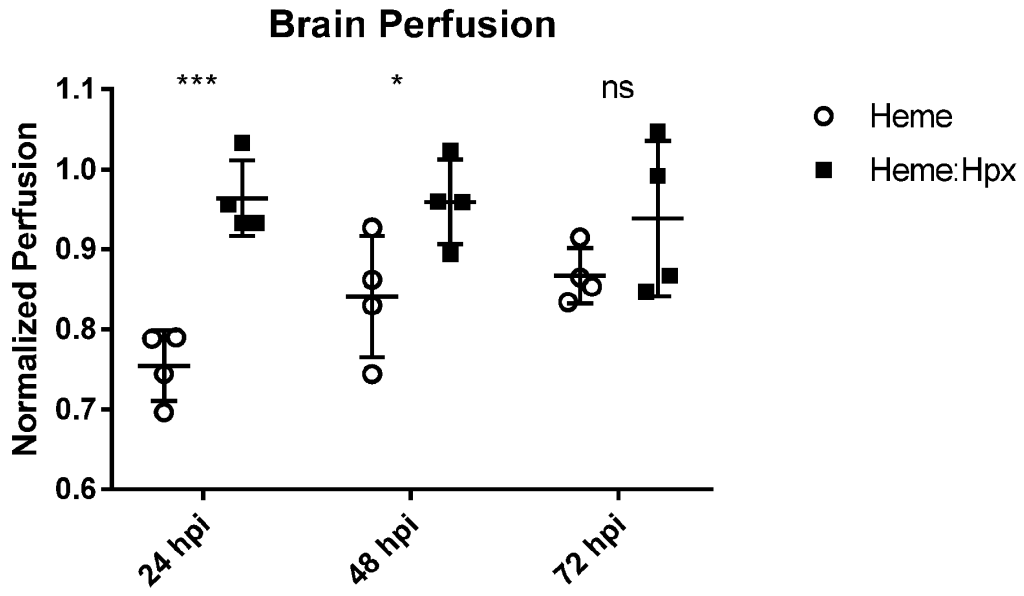

A
T2 RARE
ADC-map
ASL-Perfusion
B
T2 RARE
ADC-map
ASL-Perfusion

Figure 14

A


Lesion Size in T2w MRI sequence
Lesion size (% of hemisphere)
15
10
5
0
****
****
***
24 hpi
48 hpi
72 hpi
Heme
Heme:Hpx

B


Brain Perfusion
Normalized Perfusion
1.1
1.0
0.9
0.8
0.7
0.6
***
*
ns
24 hpi
48 hpi
72 hpi
Heme
Heme:Hpx