Figure 1

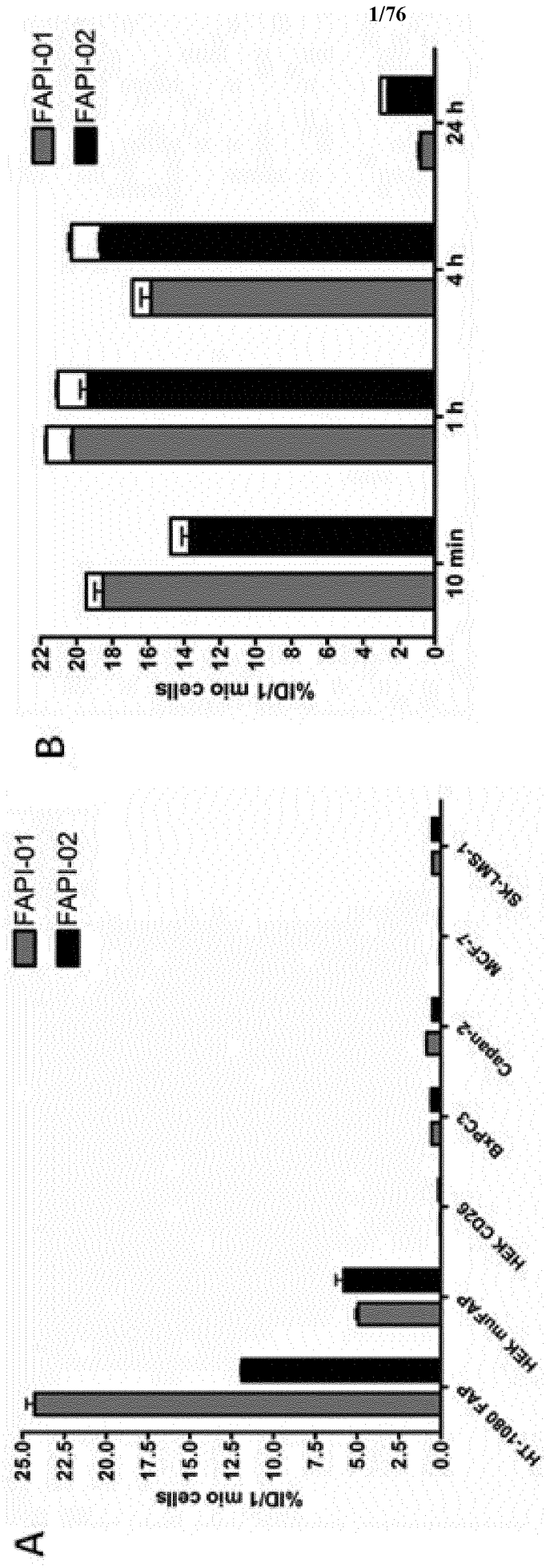

A
%ID/1 mio cells
25.0
22.5
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
FAPI-01
FAPI-02
HT-1080 FAP
HEK muFAP
HEK CD26
BxPC3
Capan-2
MCF-7
SK-LMS-1
B
%ID/1 mio cells
22
20
18
16
14
12
10
8
6
4
2
0
FAPI-01
FAPI-02
10 min
1 h
4 h
24 h

Figure 1 continued

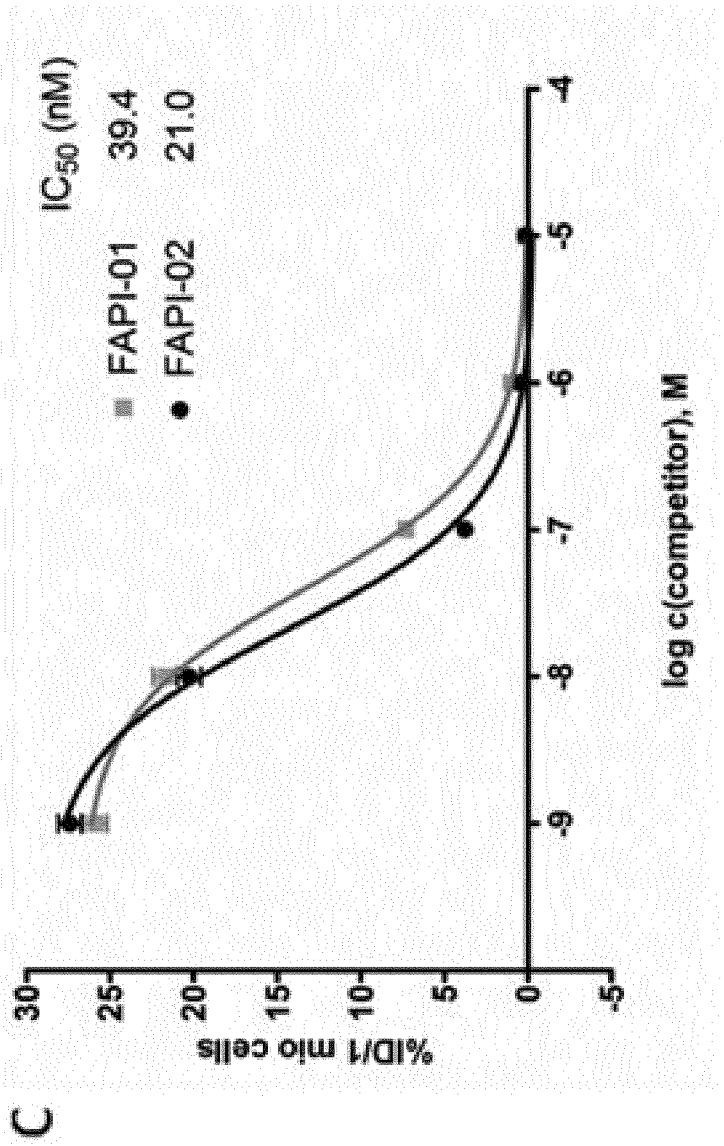


Figure 1 continued

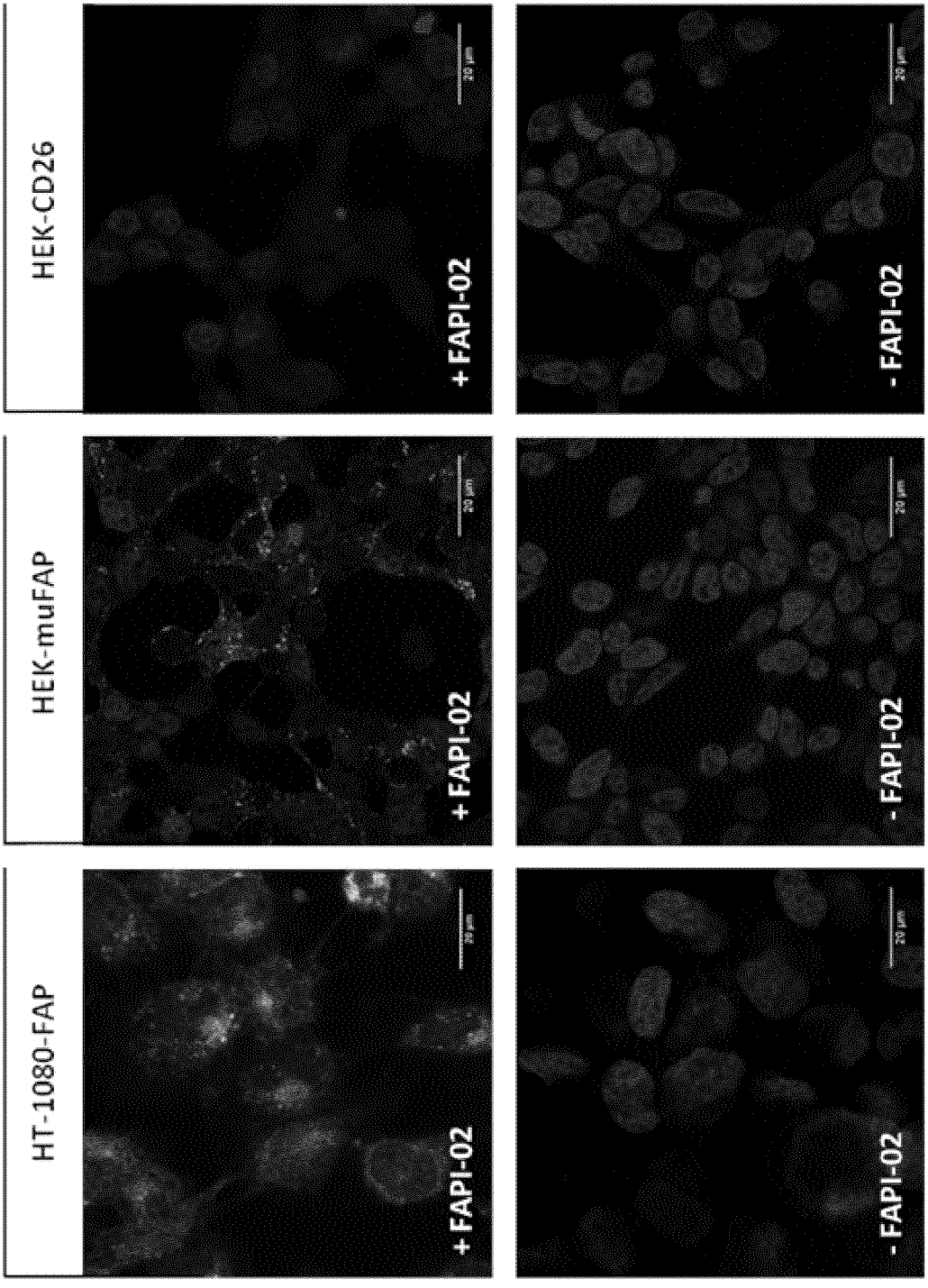


Figure 1 continued

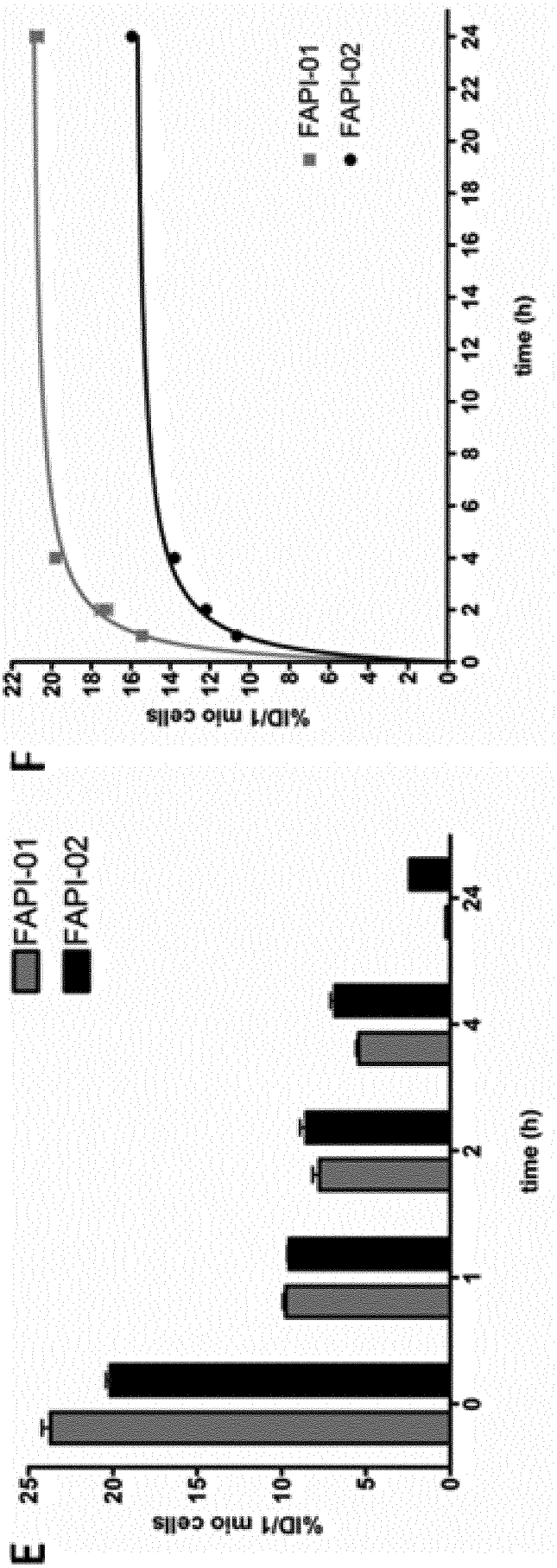


Figure 2

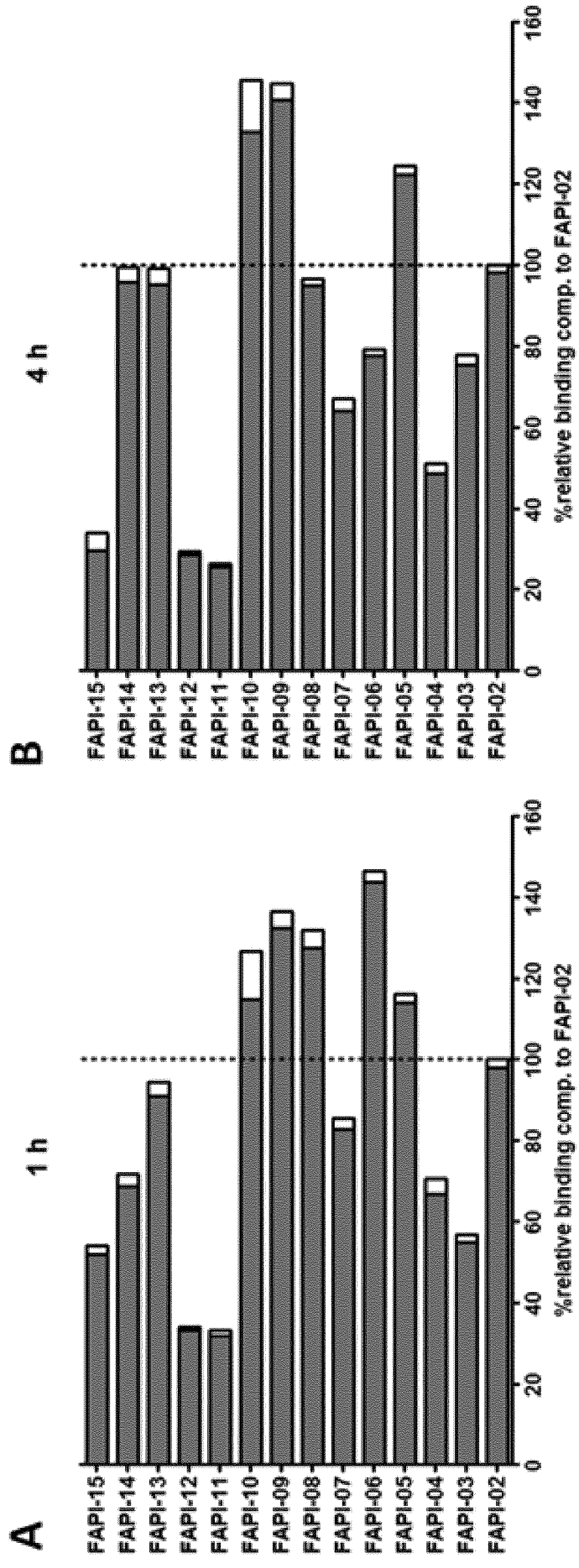

A
1 h
B
4 h
FAPI-15
FAPI-14
FAPI-13
FAPI-12
FAPI-11
FAPI-10
FAPI-09
FAPI-08
FAPI-07
FAPI-06
FAPI-05
FAPI-04
FAPI-03
FAPI-02
0
20
40
60
80
100
120
140
160
%relative binding comp. to FAPI-02

Figure 2 continued

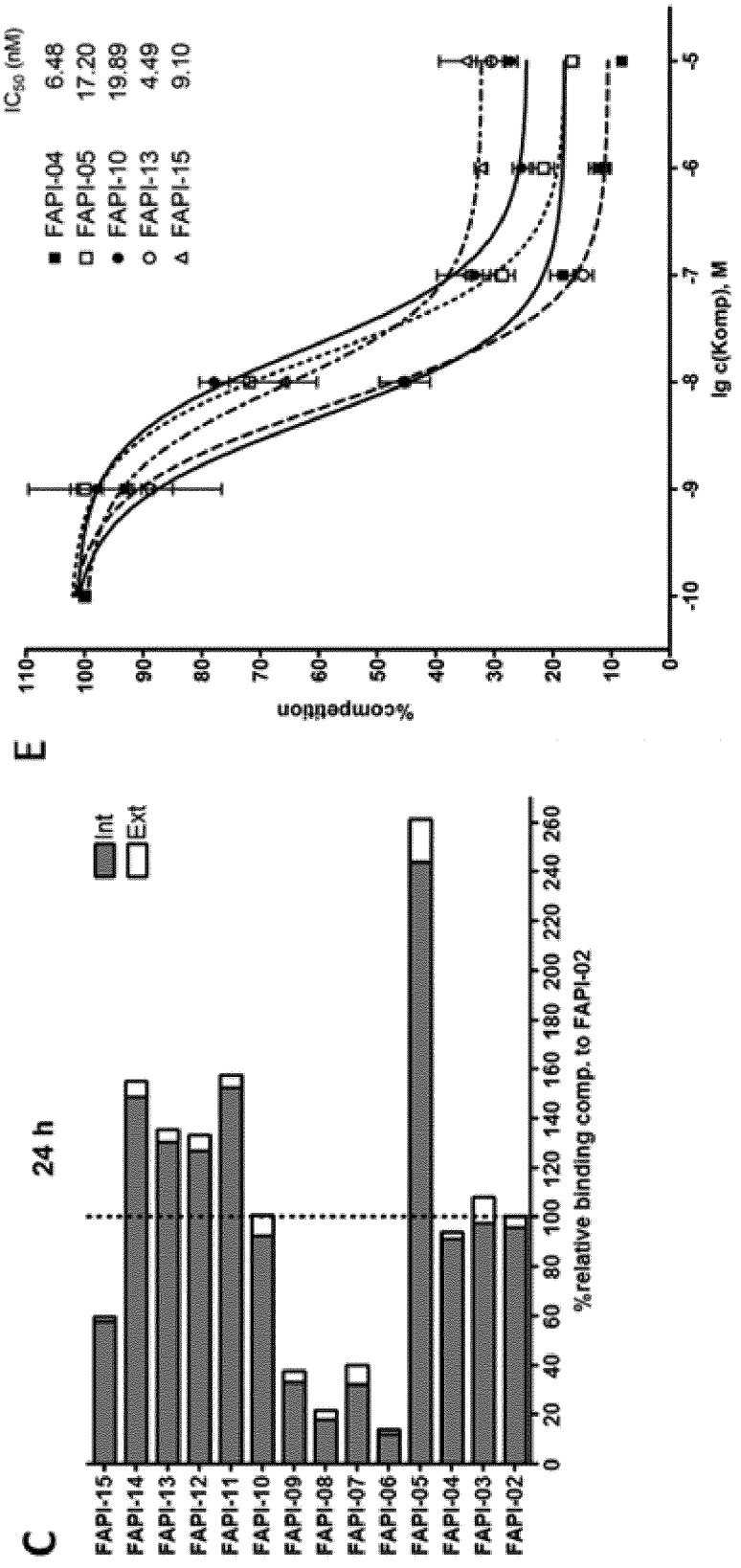


Figure 2 continued

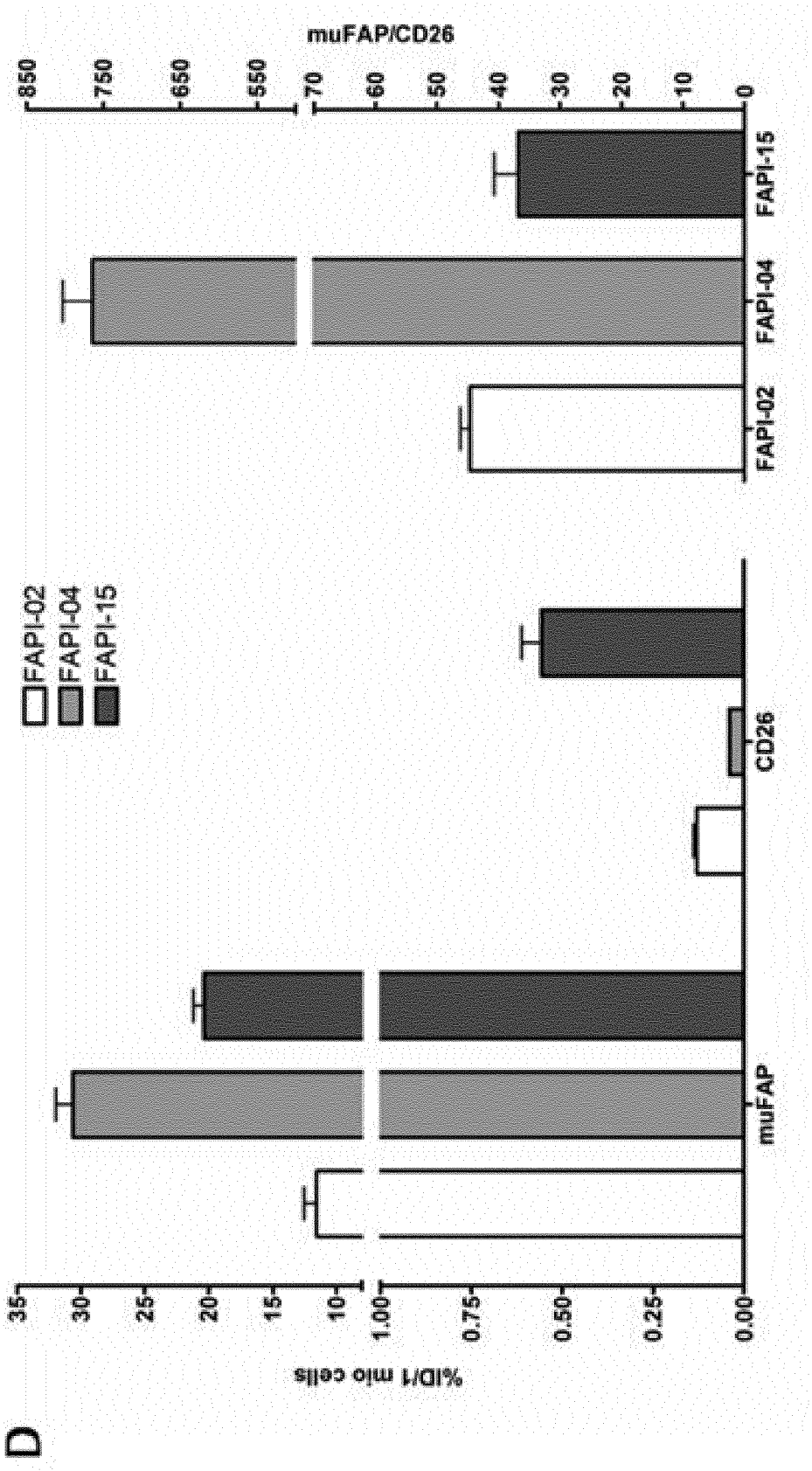


Figure 3

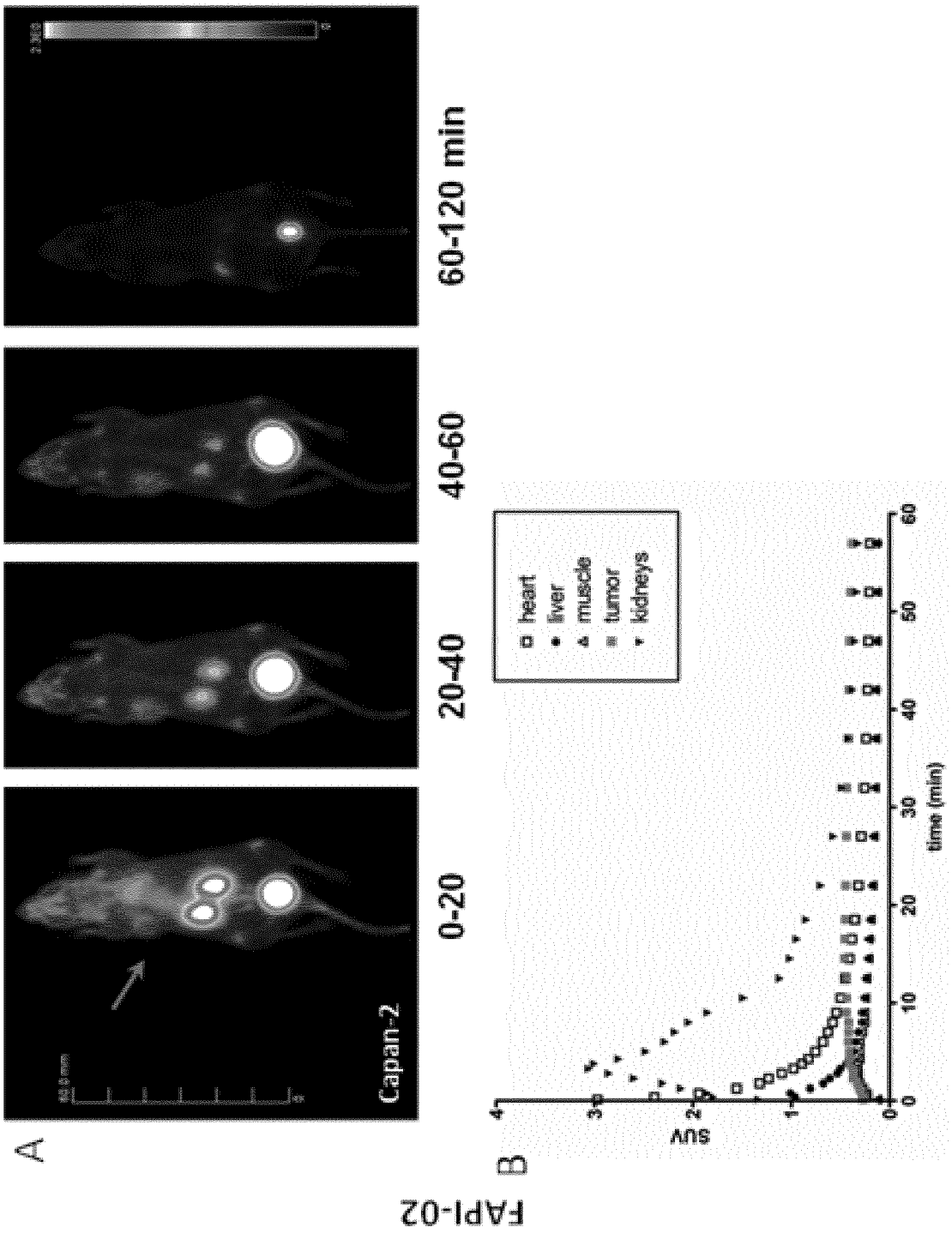

A
Capan-2
0-20
20-40
40-60
60-120 min
FAPI-02
B
heart
liver
muscle
tumor
kidneys
SUV
time (min)

Figure 3 continued

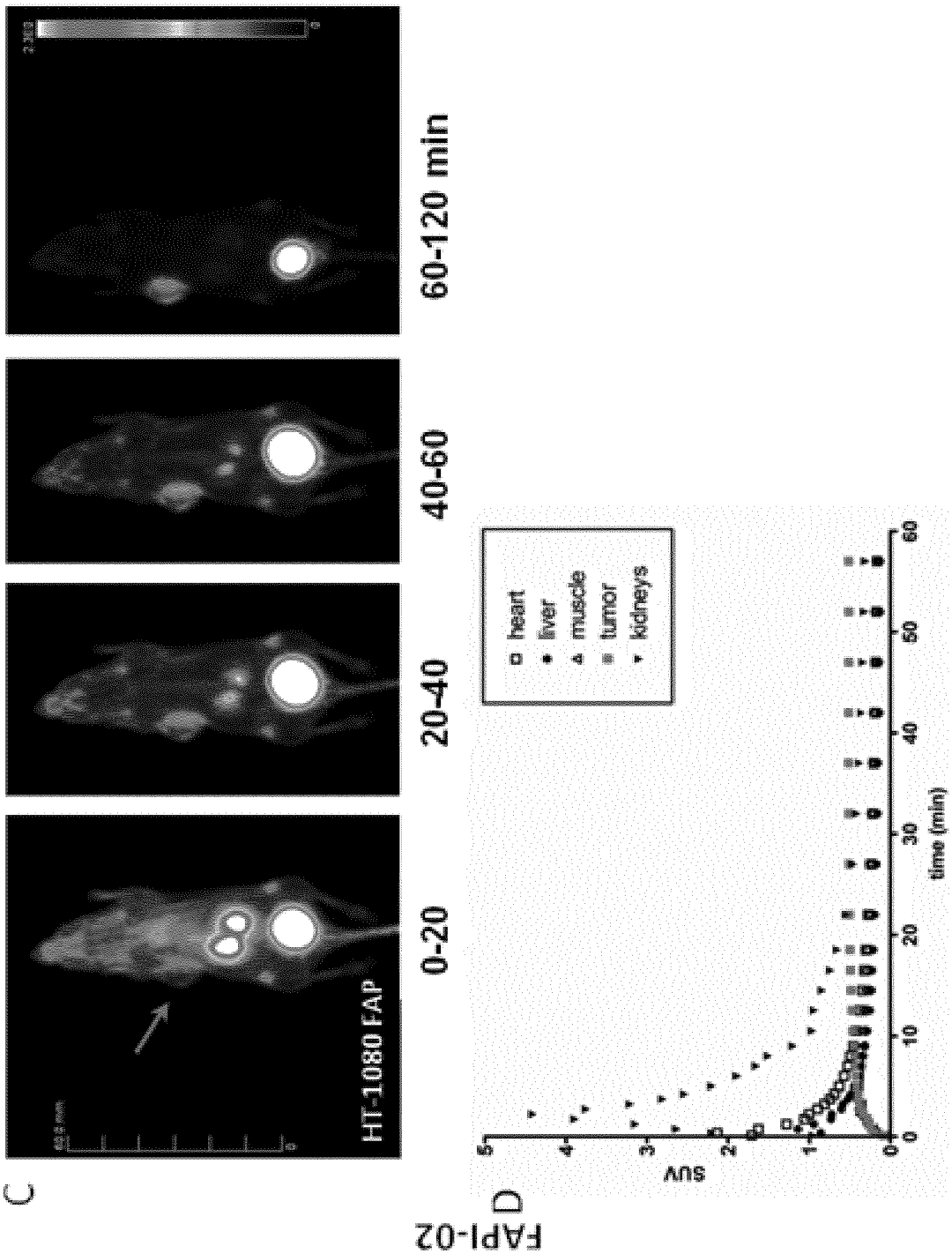


Figure 3 continued

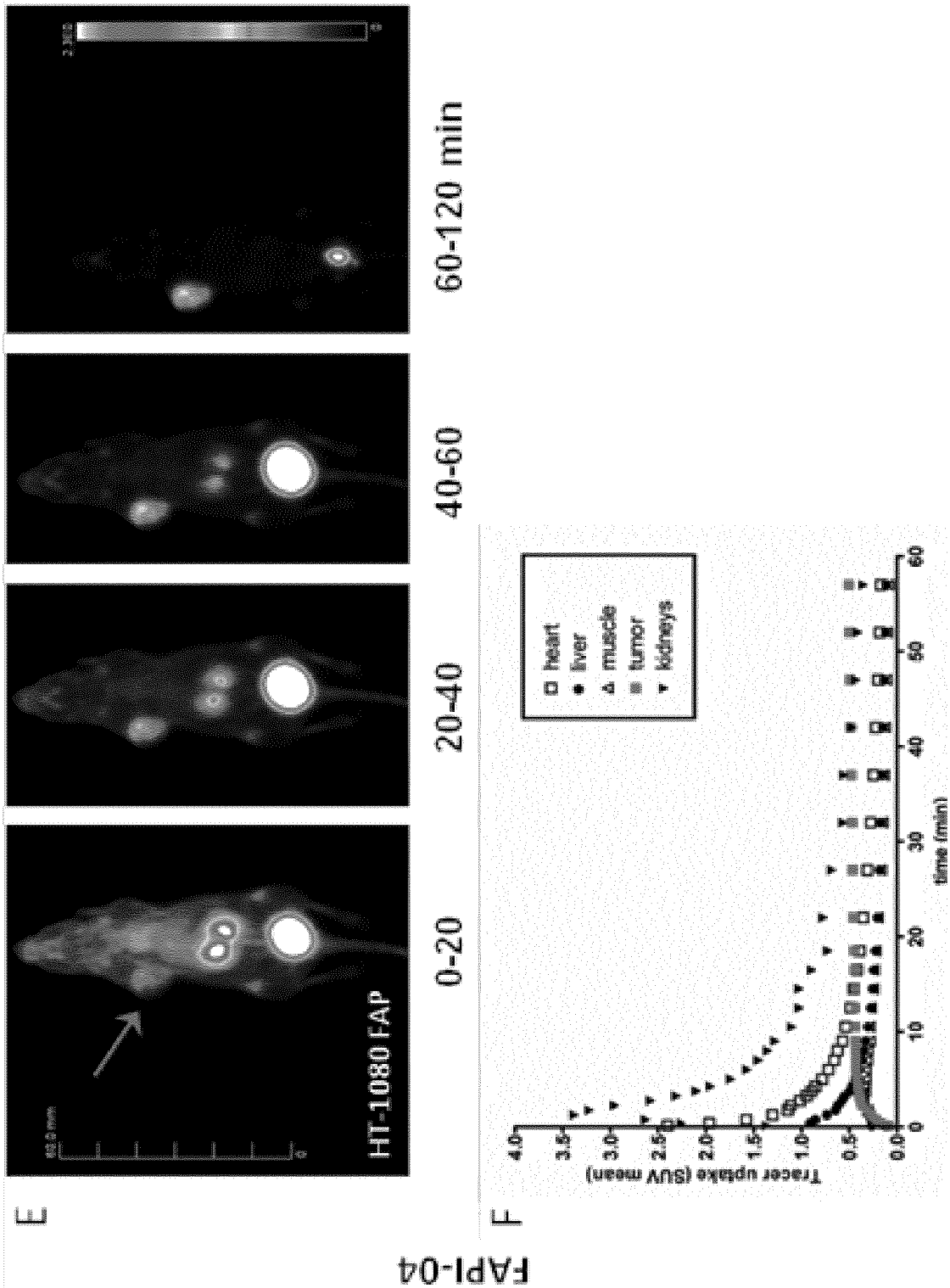


Figure 3 continued

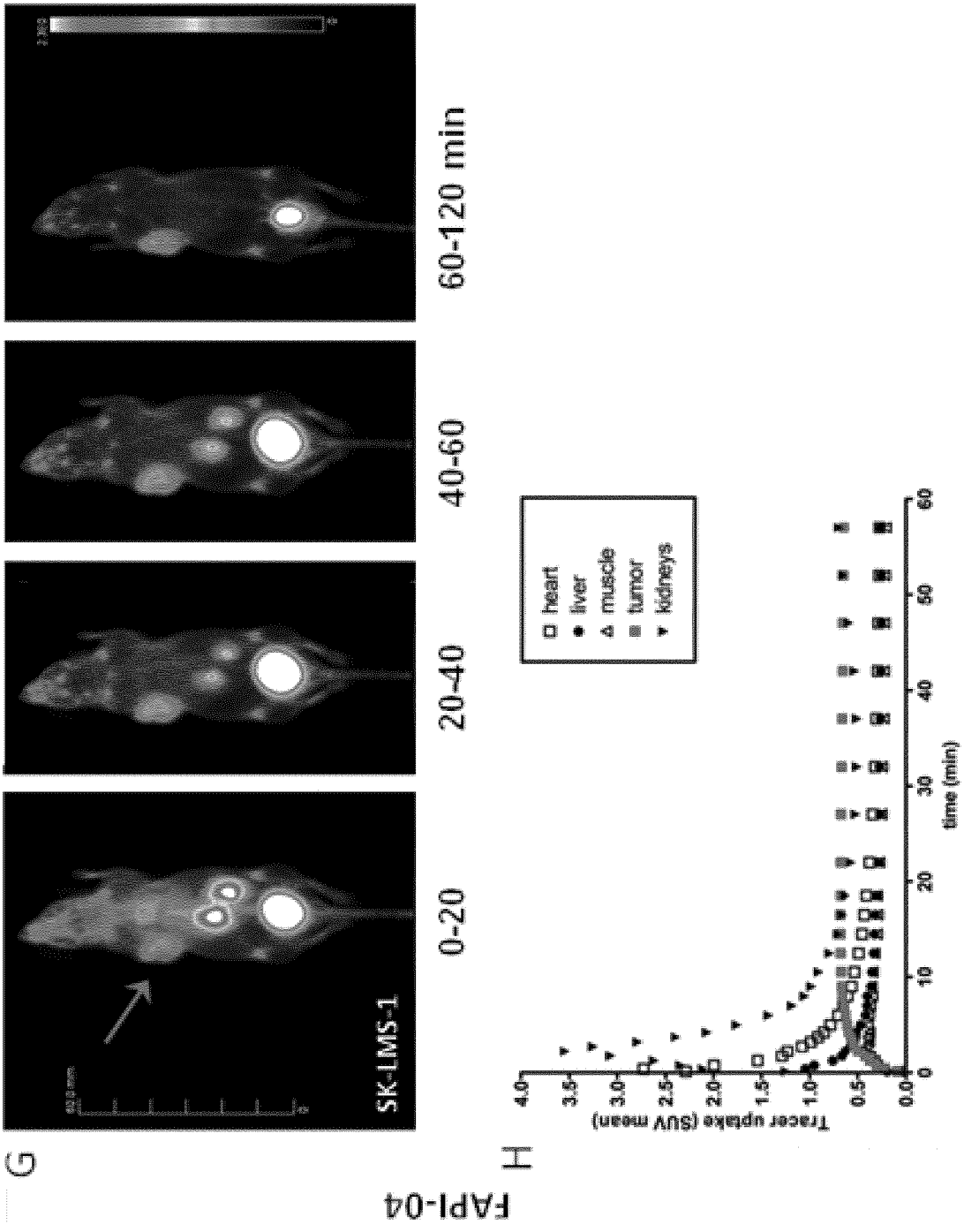


Figure 4

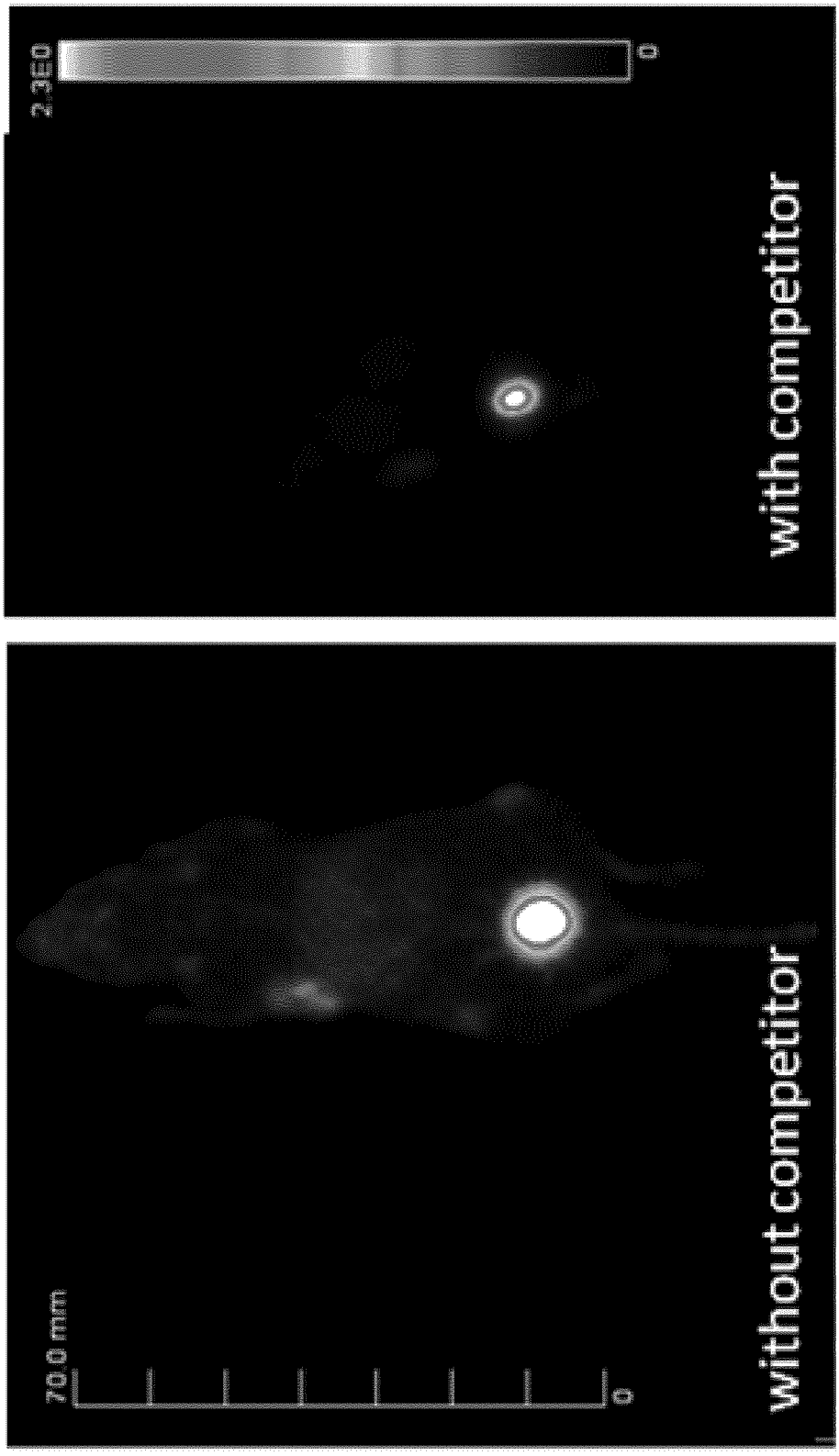


Figure 4 continued

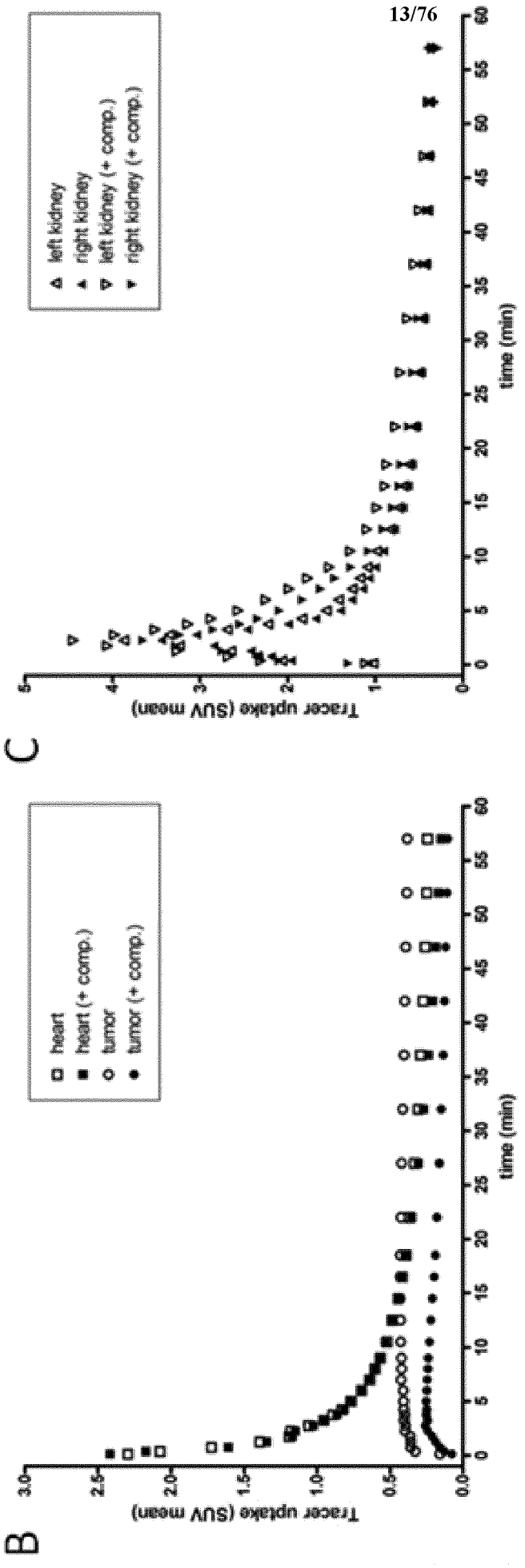


Figure 4 continued

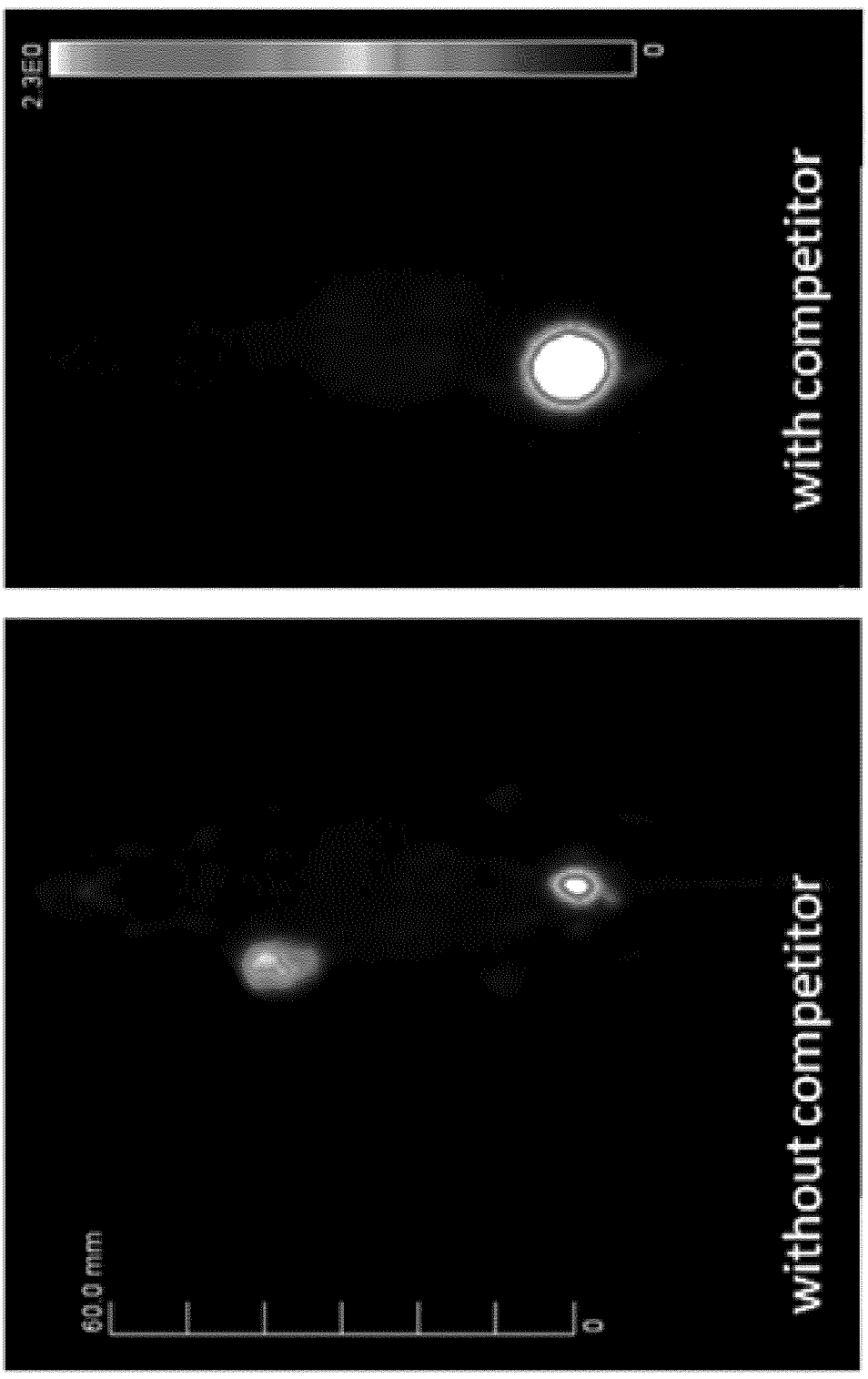


Figure 4 continued

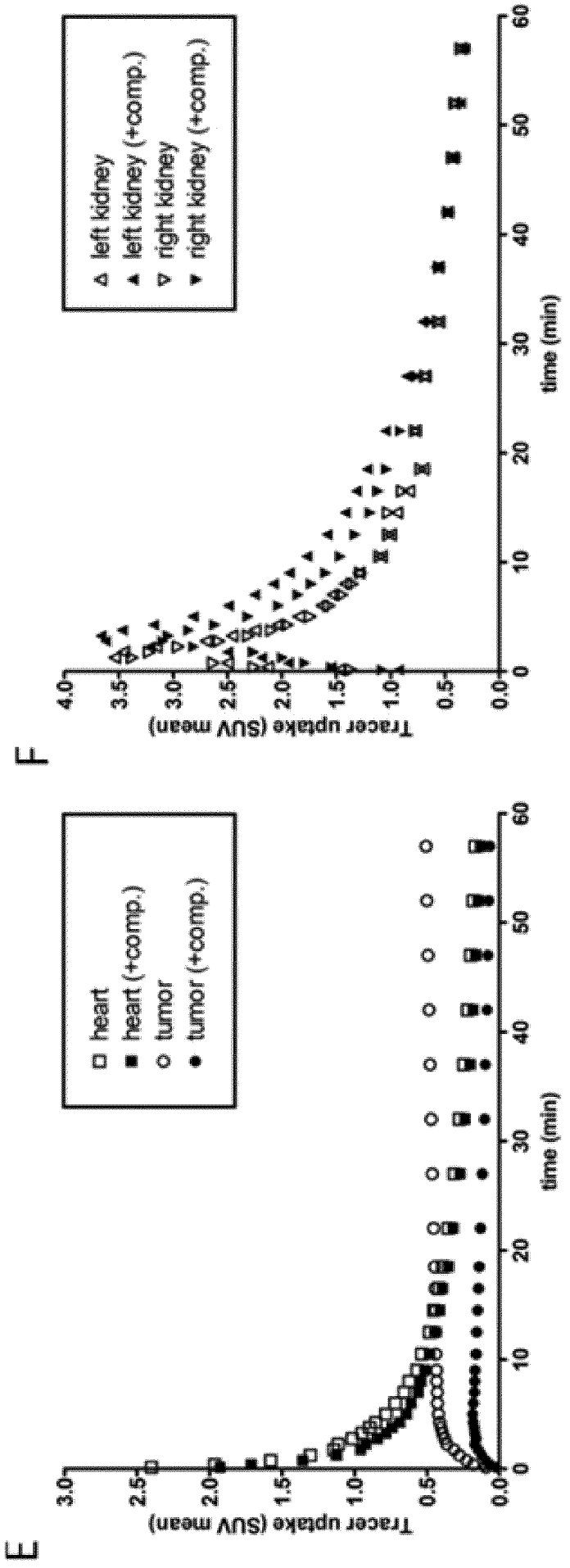


Figure 5

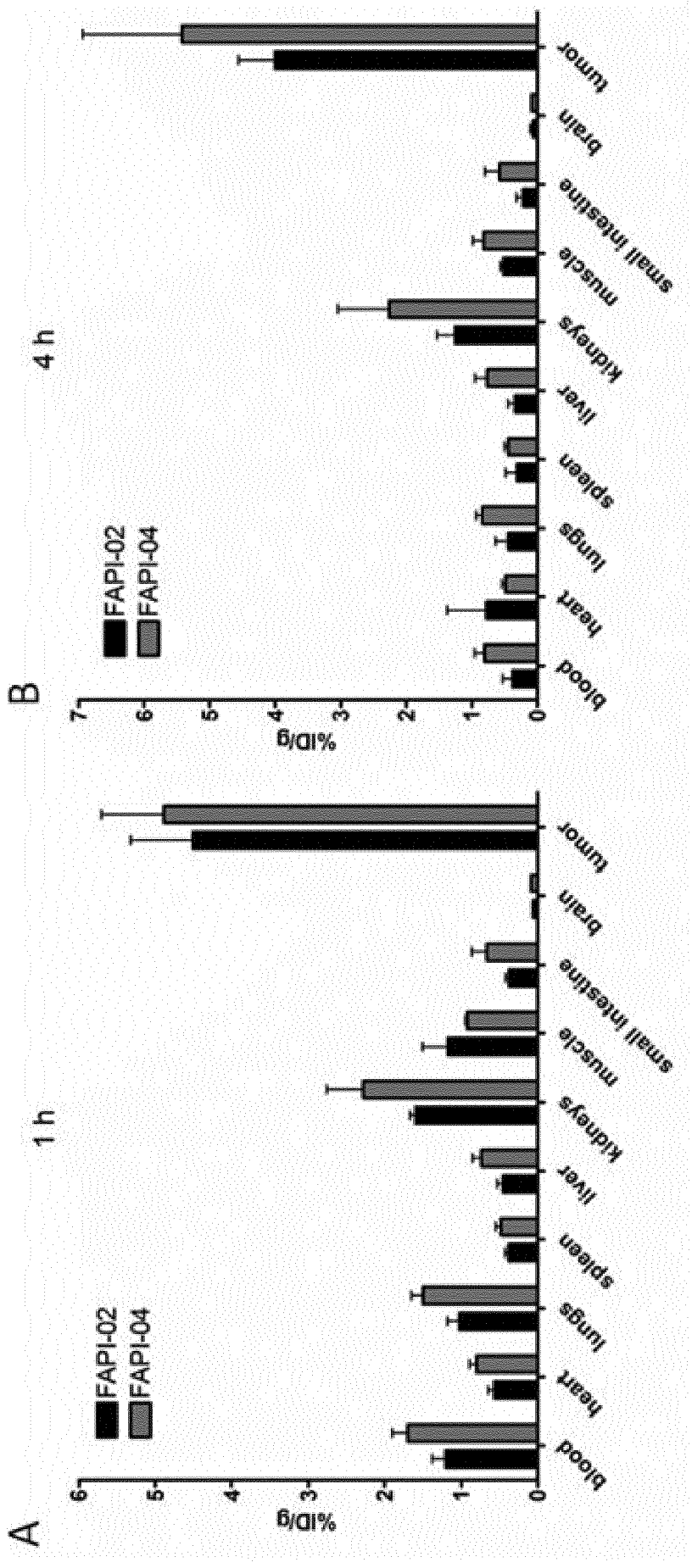

A
1 h
%ID/g
FAPI-02
FAPI-04
blood
heart
lungs
spleen
liver
kidneys
muscle
small intestine
brain
tumor
B
4 h
%ID/g
FAPI-02
FAPI-04
blood
heart
lungs
spleen
liver
kidneys
muscle
small intestine
brain
tumor

Figure 5 continued

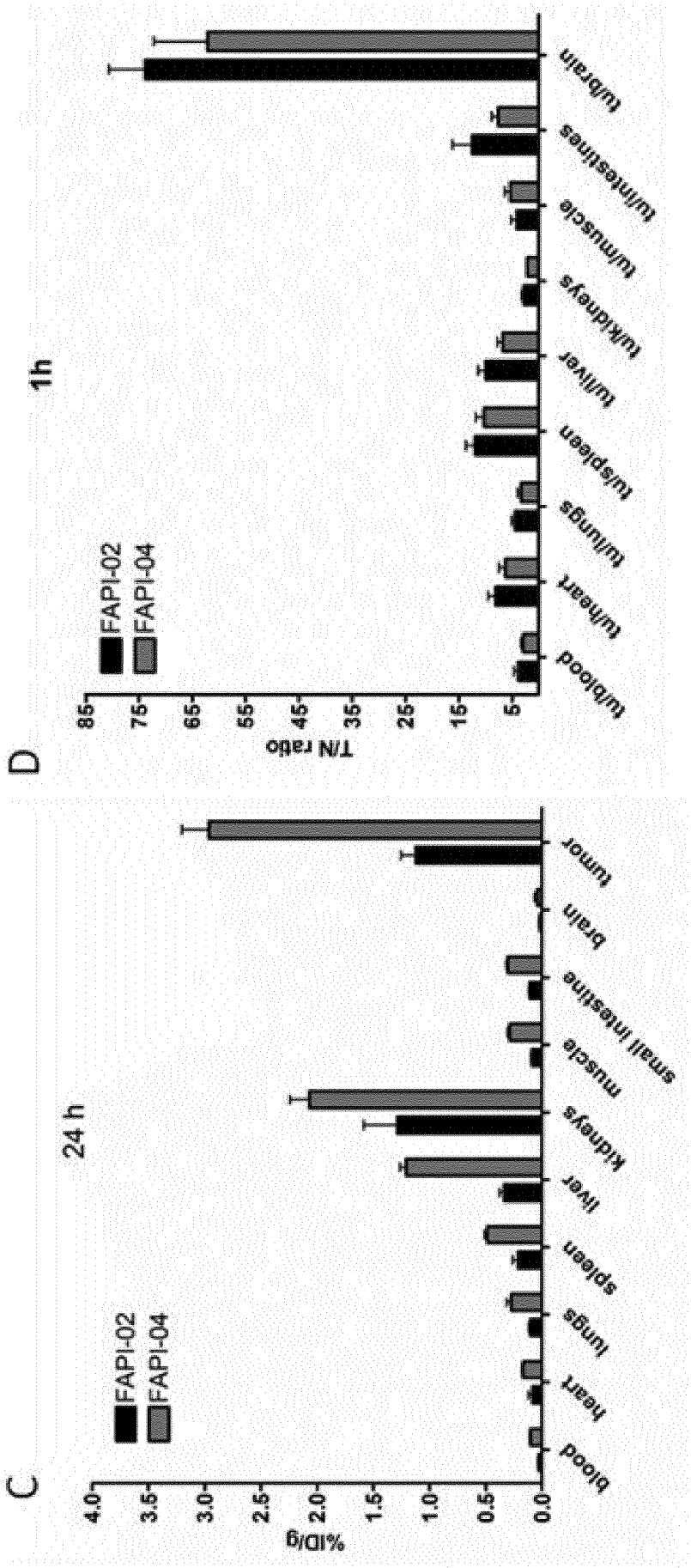


Figure 5 continued

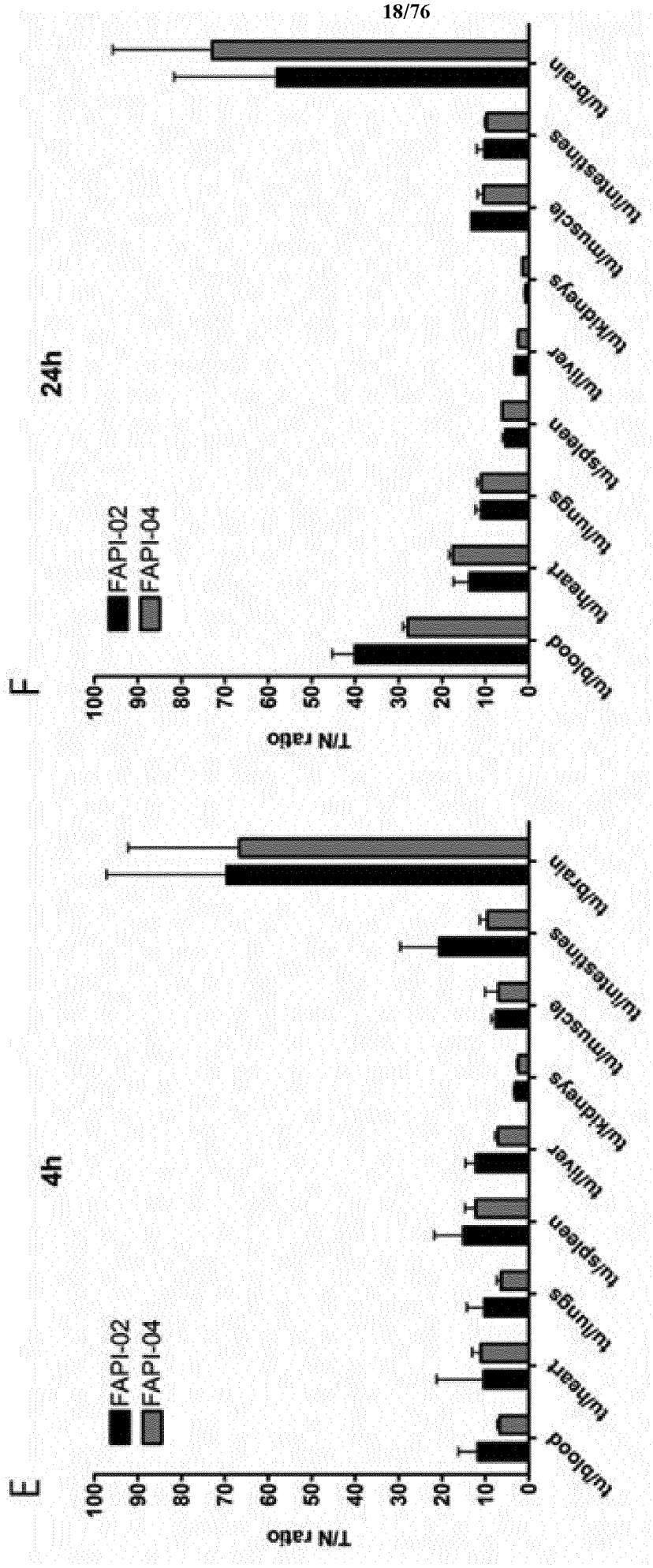


Figure 6

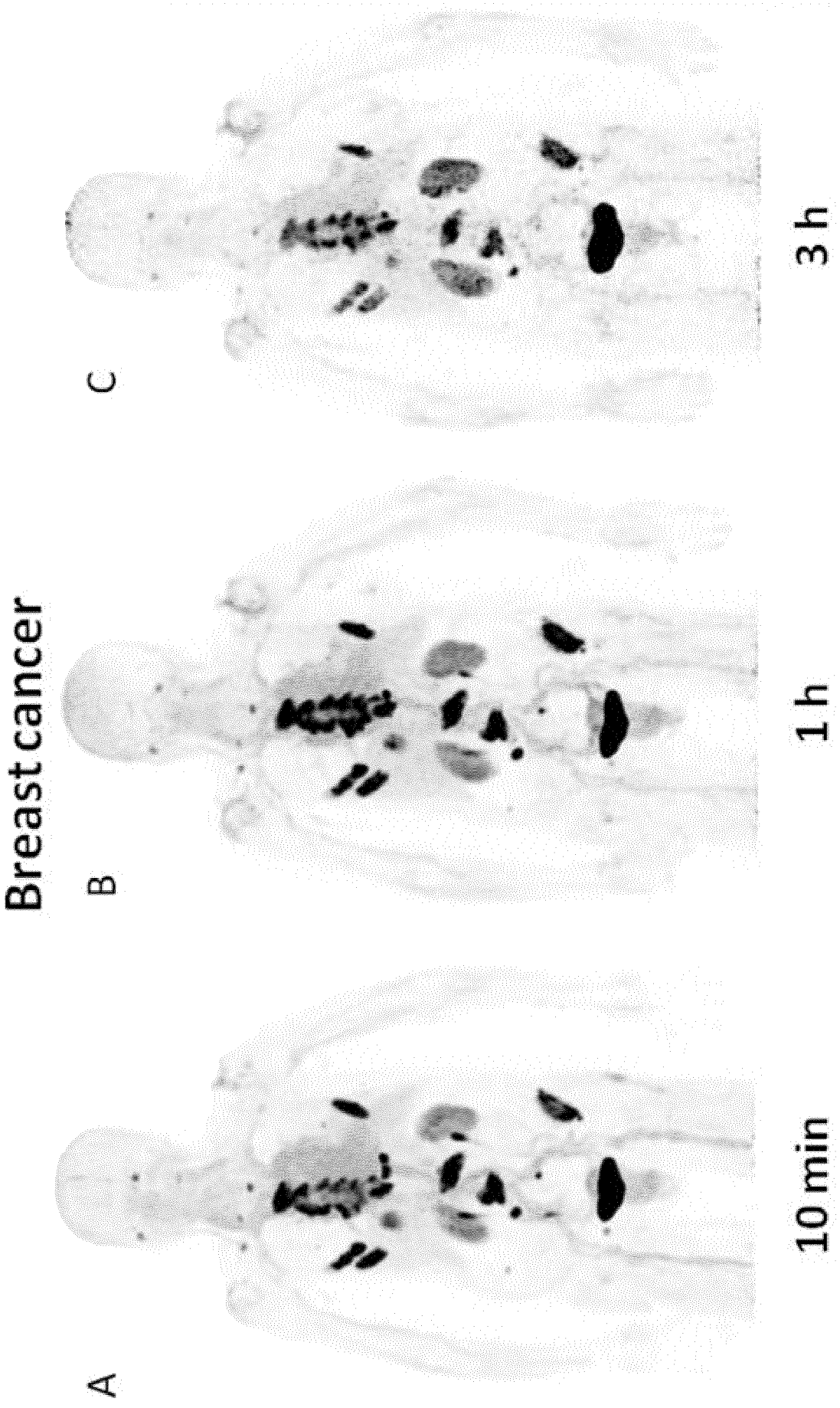


Figure 6 continued

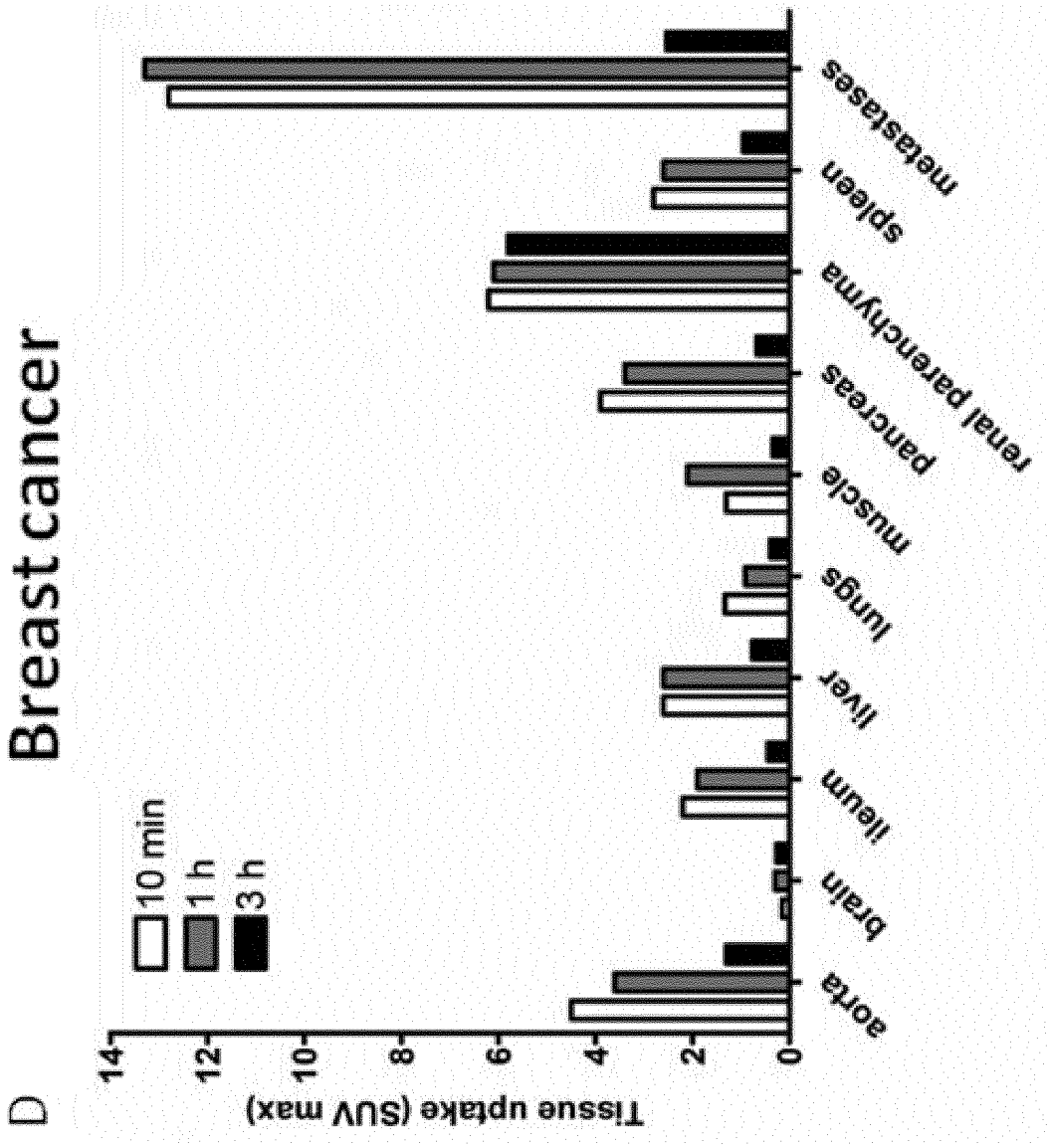


Figure 7

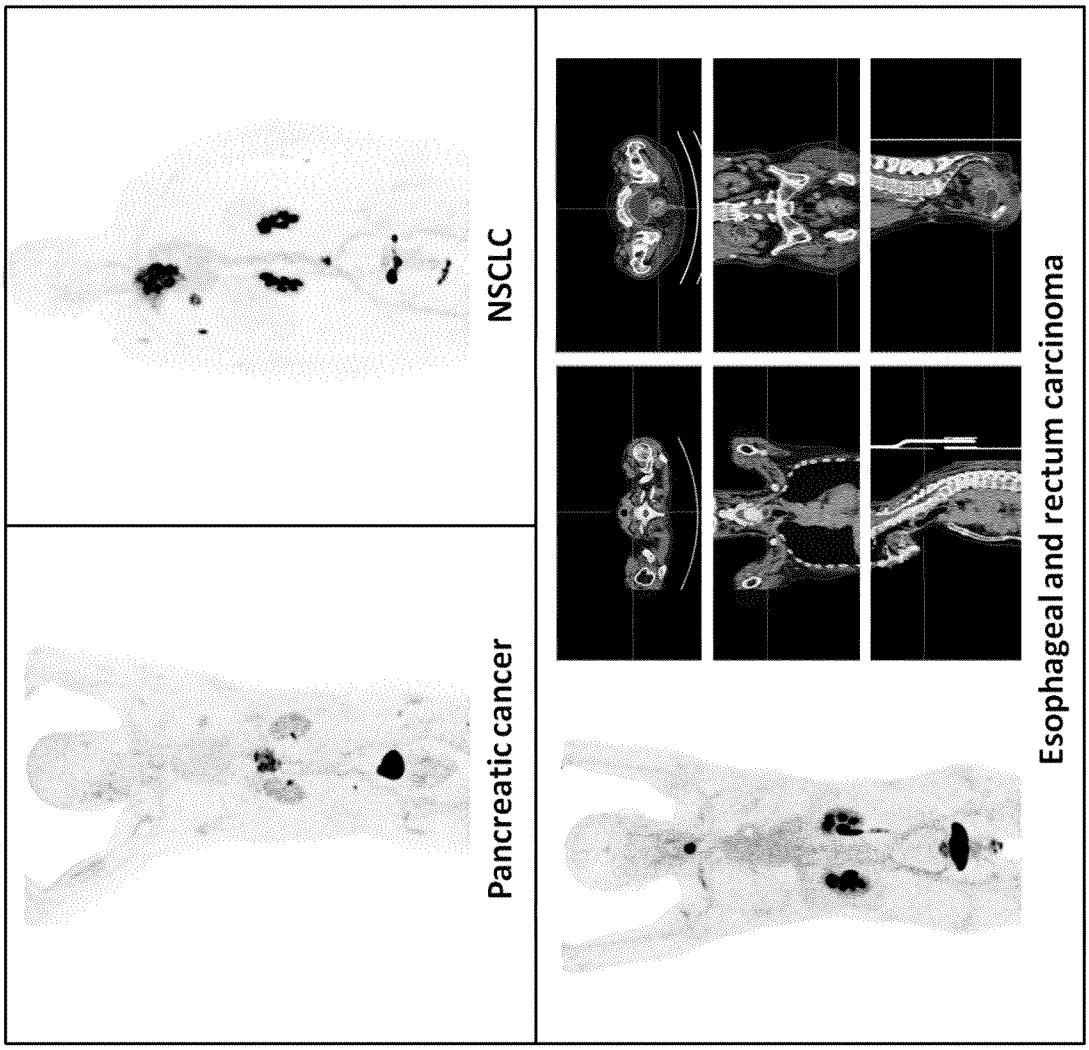


Figure 8

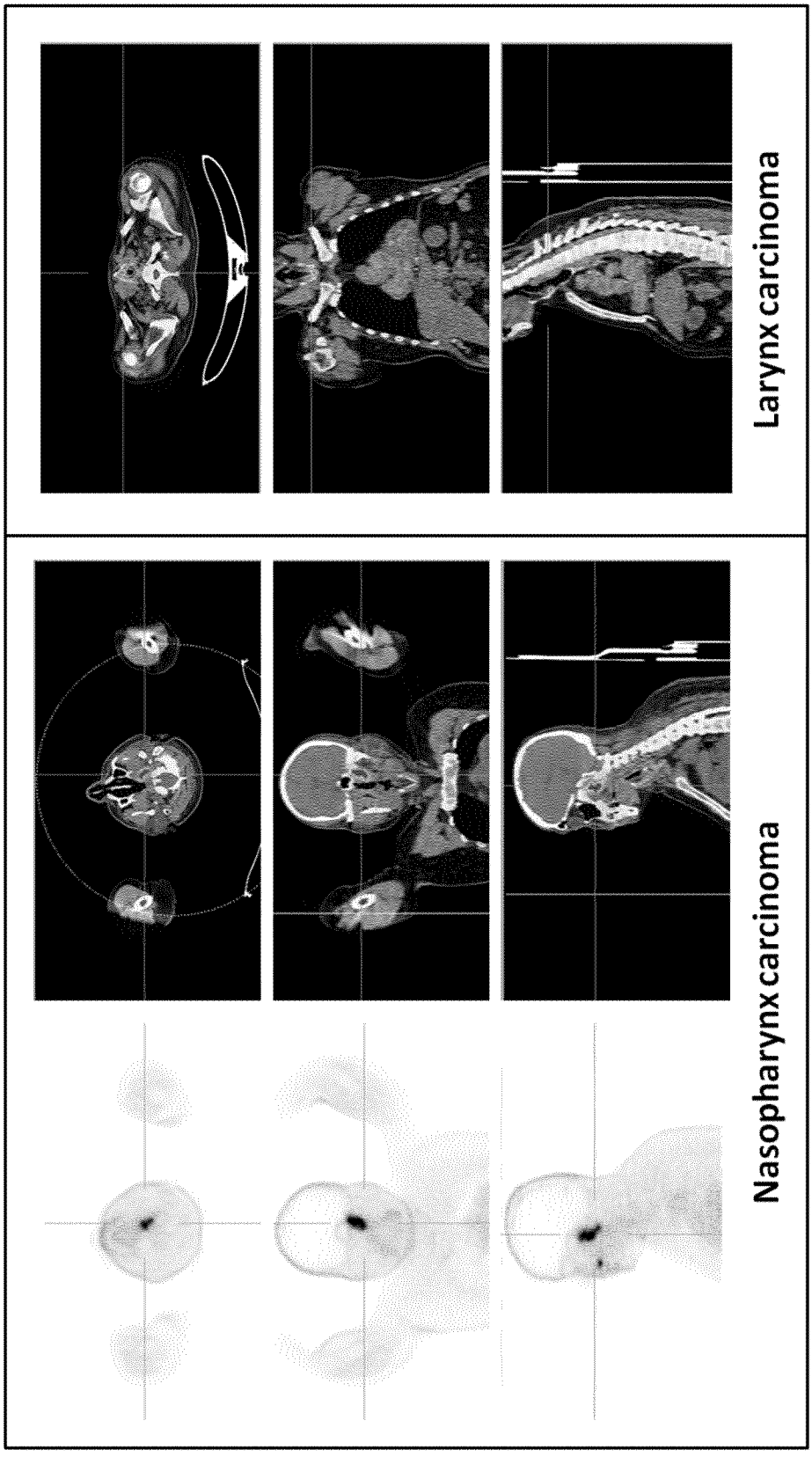


Figure 9

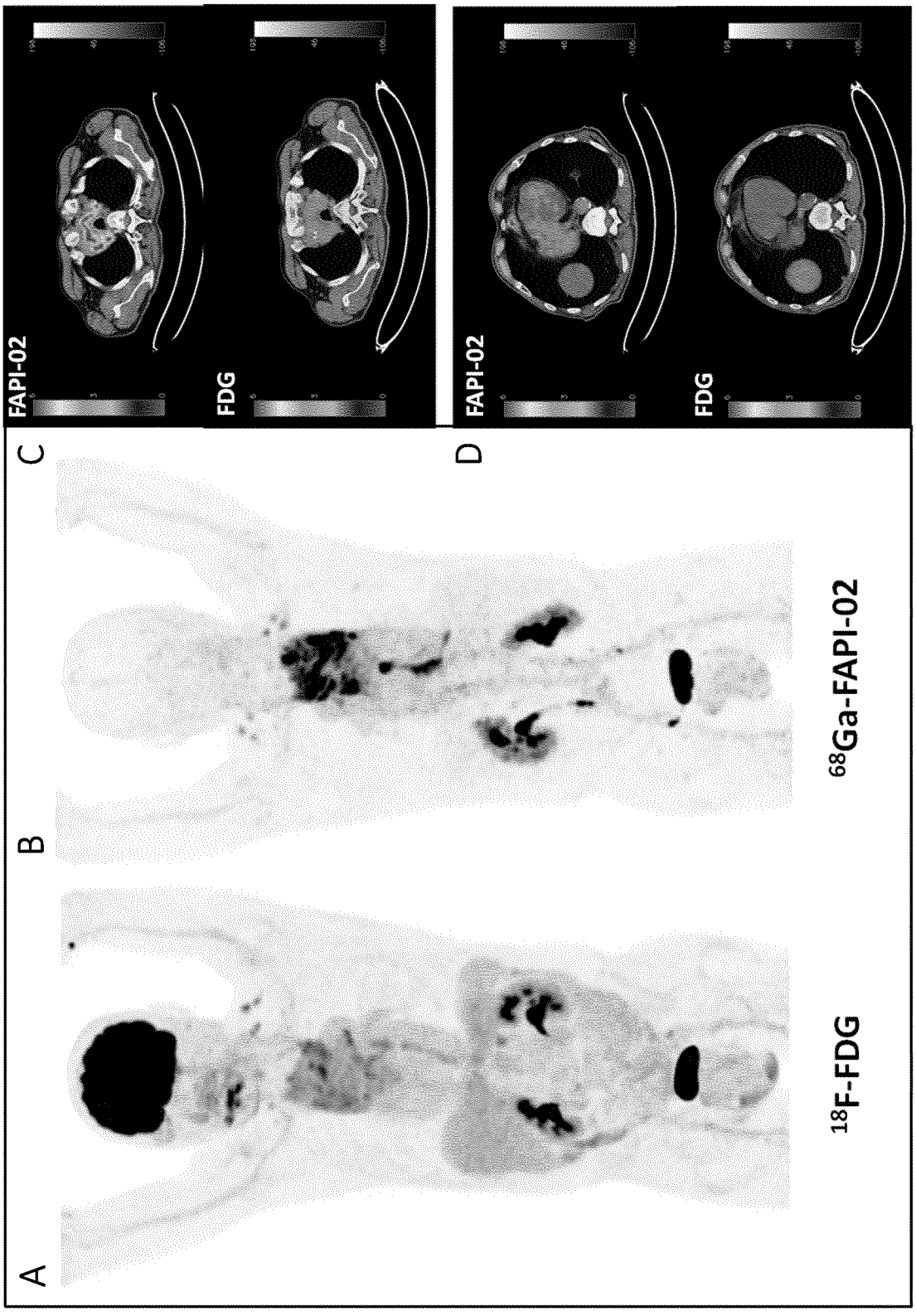


Figure 10

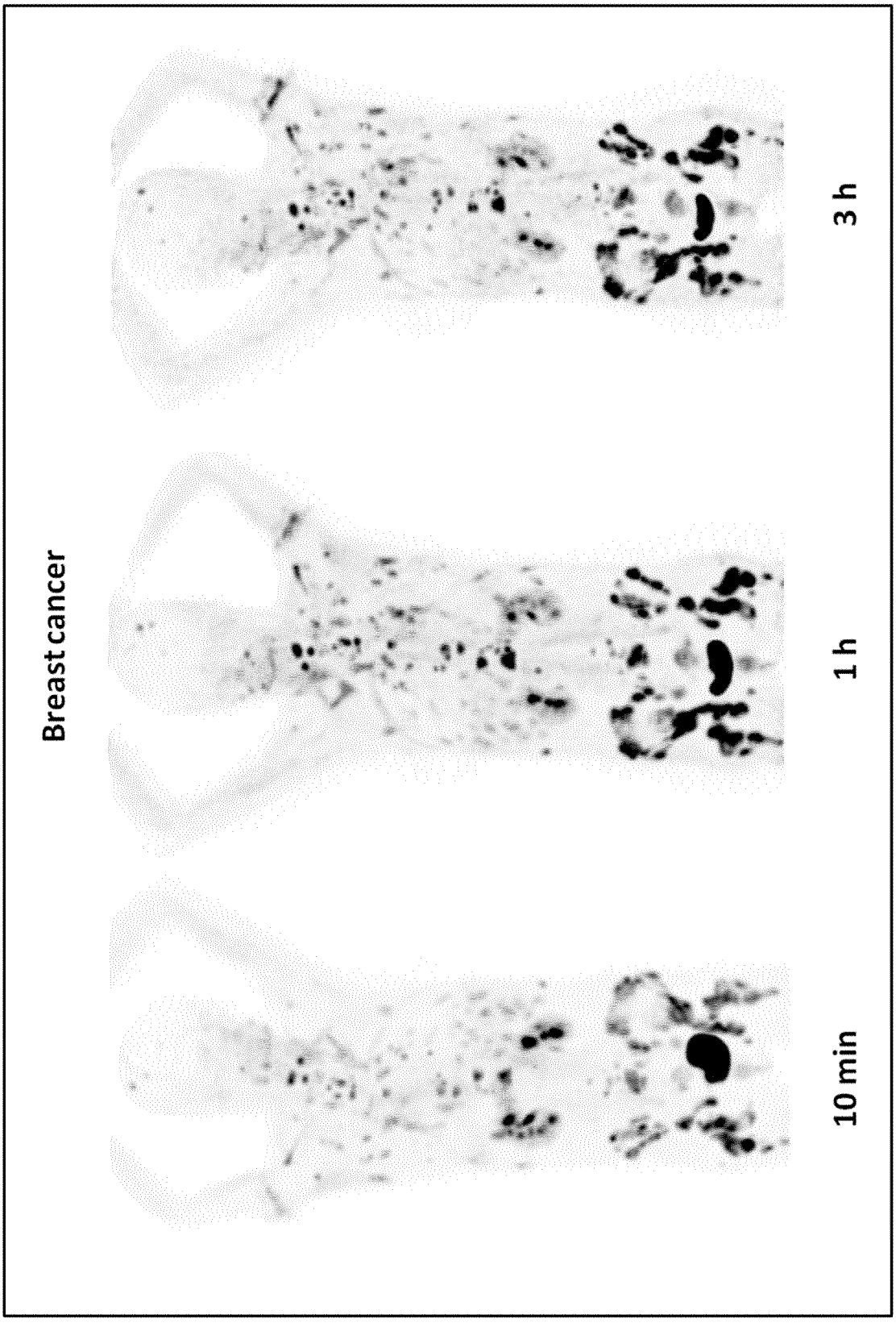


Figure 11

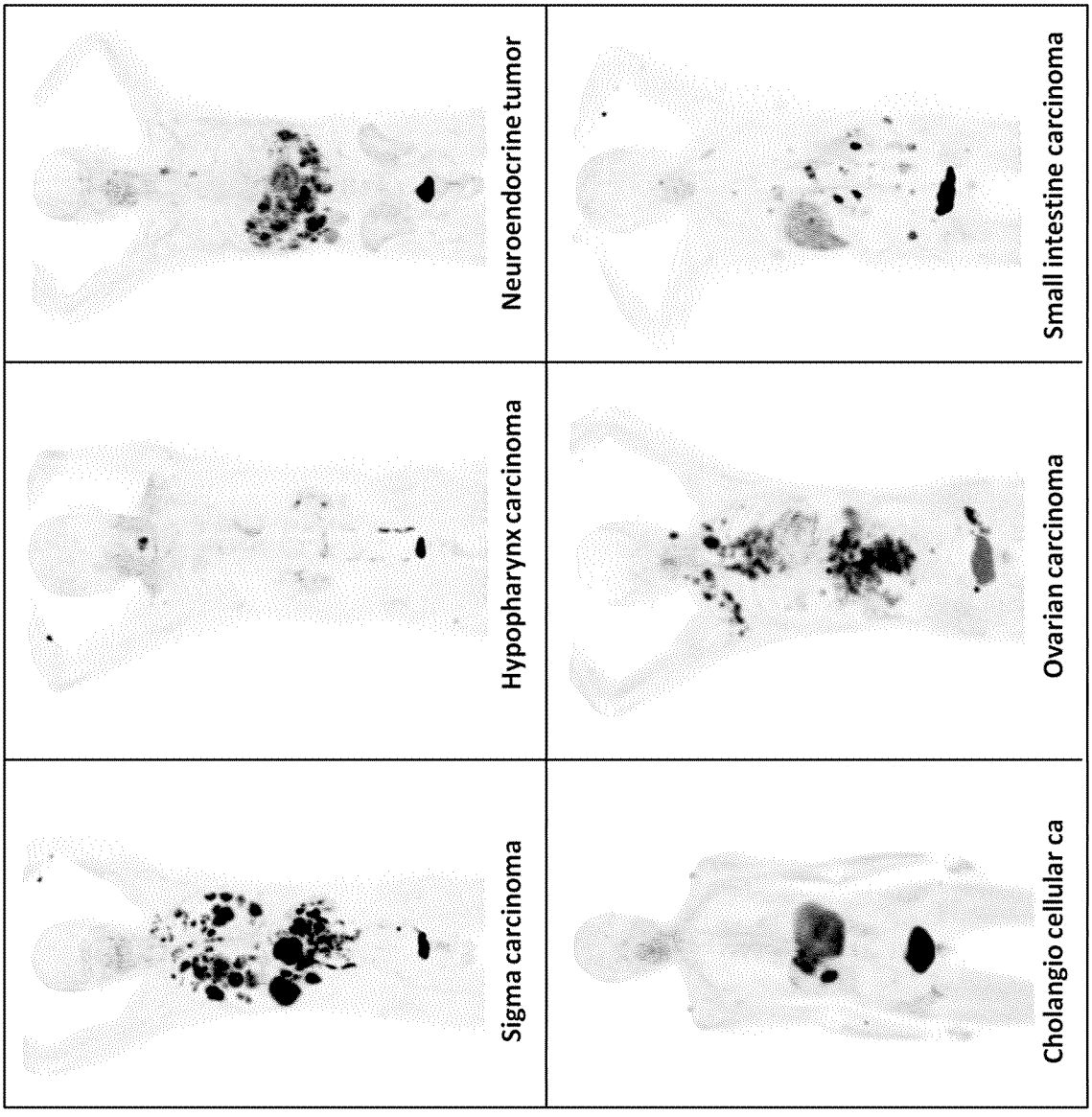

Neuroendocrine tumor
Hypopharynx carcinoma
Sigma carcinoma
Small intestine carcinoma
Ovarian carcinoma
Cholangio cellular ca

Figure 12



Figure 13

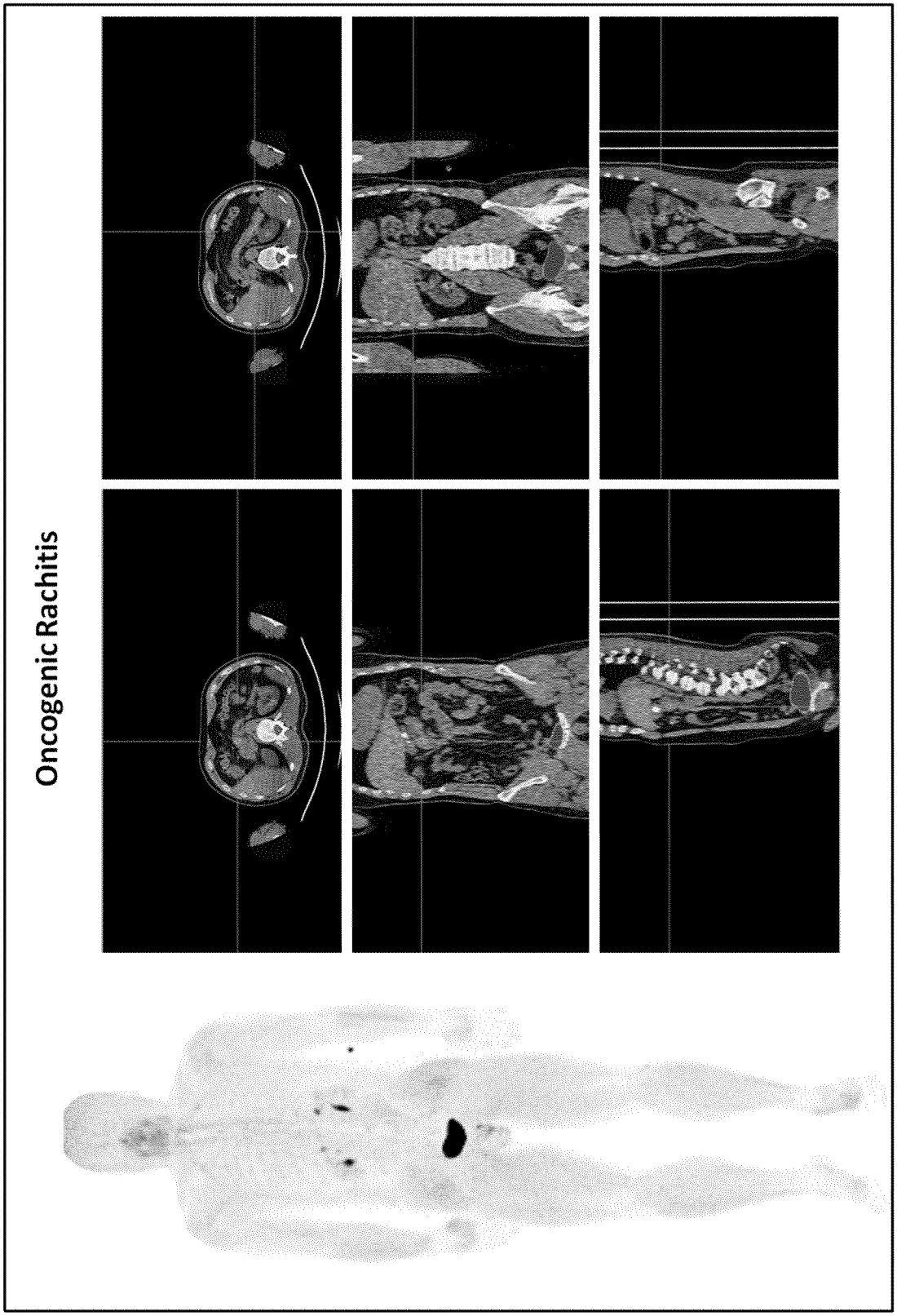


Figure 14

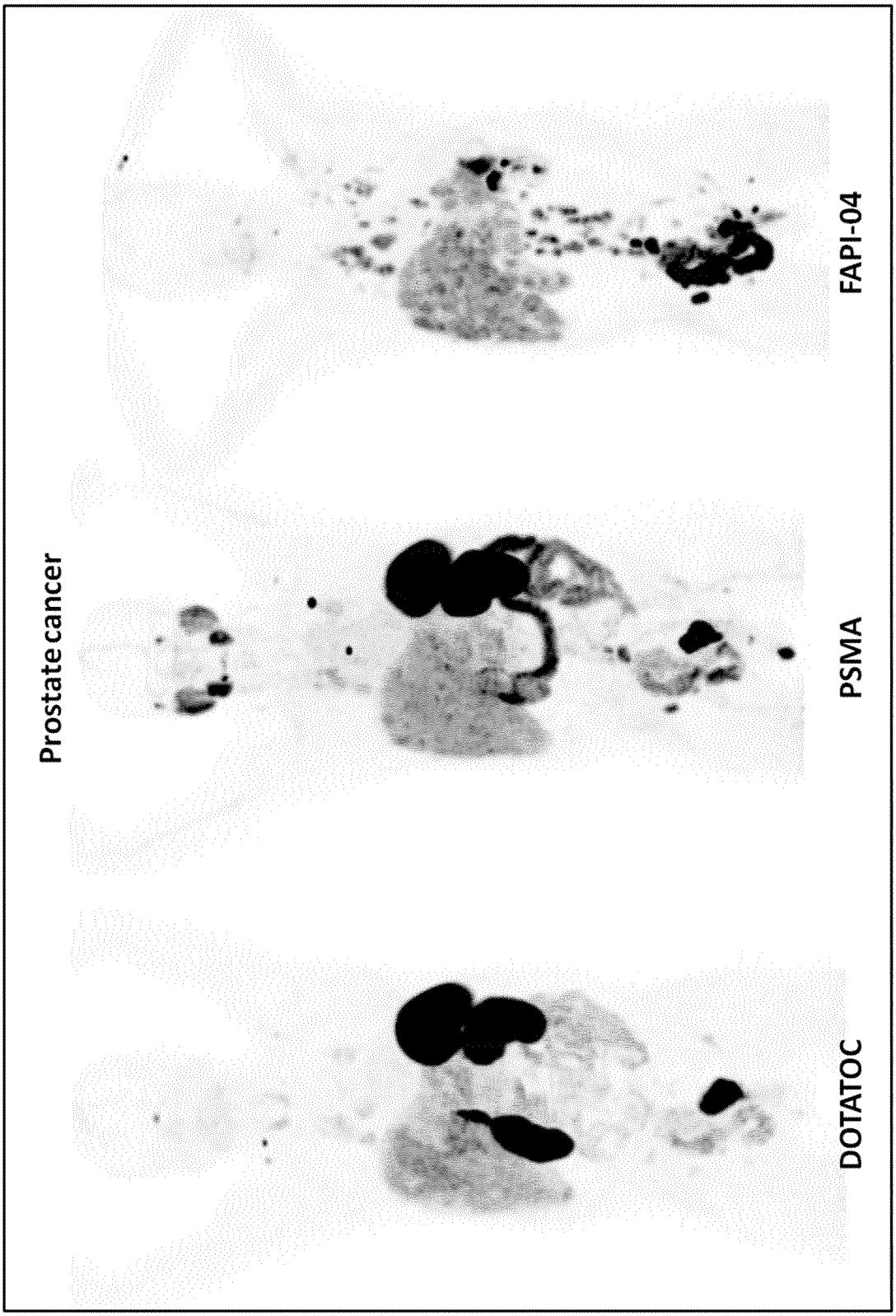


Figure 15

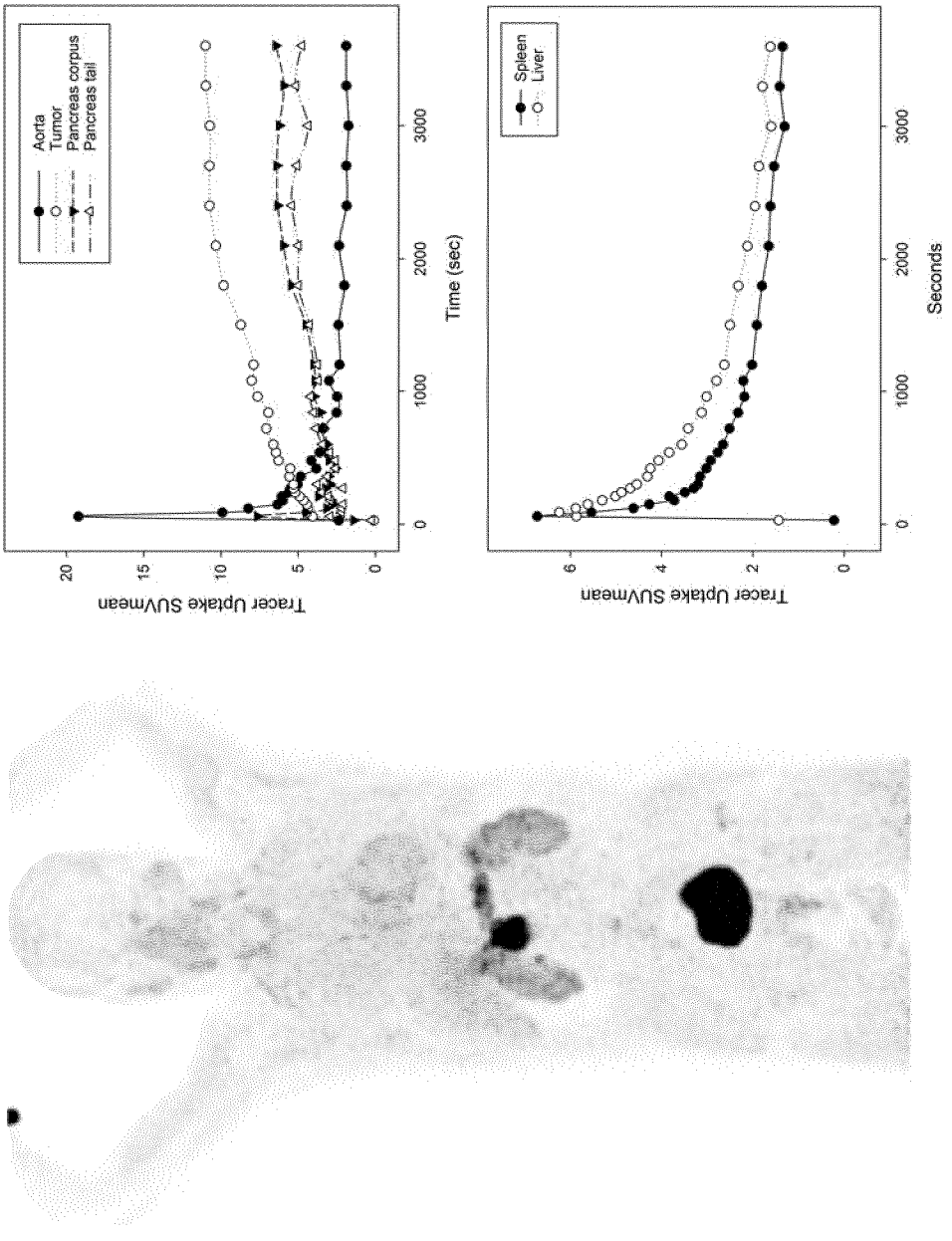

Aorta
Tumor
Pancreas corpus
Pancreas tail
Tracer Uptake SUVmean
Time (sec)
Spleen
Liver
Tracer Uptake SUVmean
Seconds
ri kidney
le kidney
Muscle
Tracer Uptake SUVmean
Seconds

Figure 16

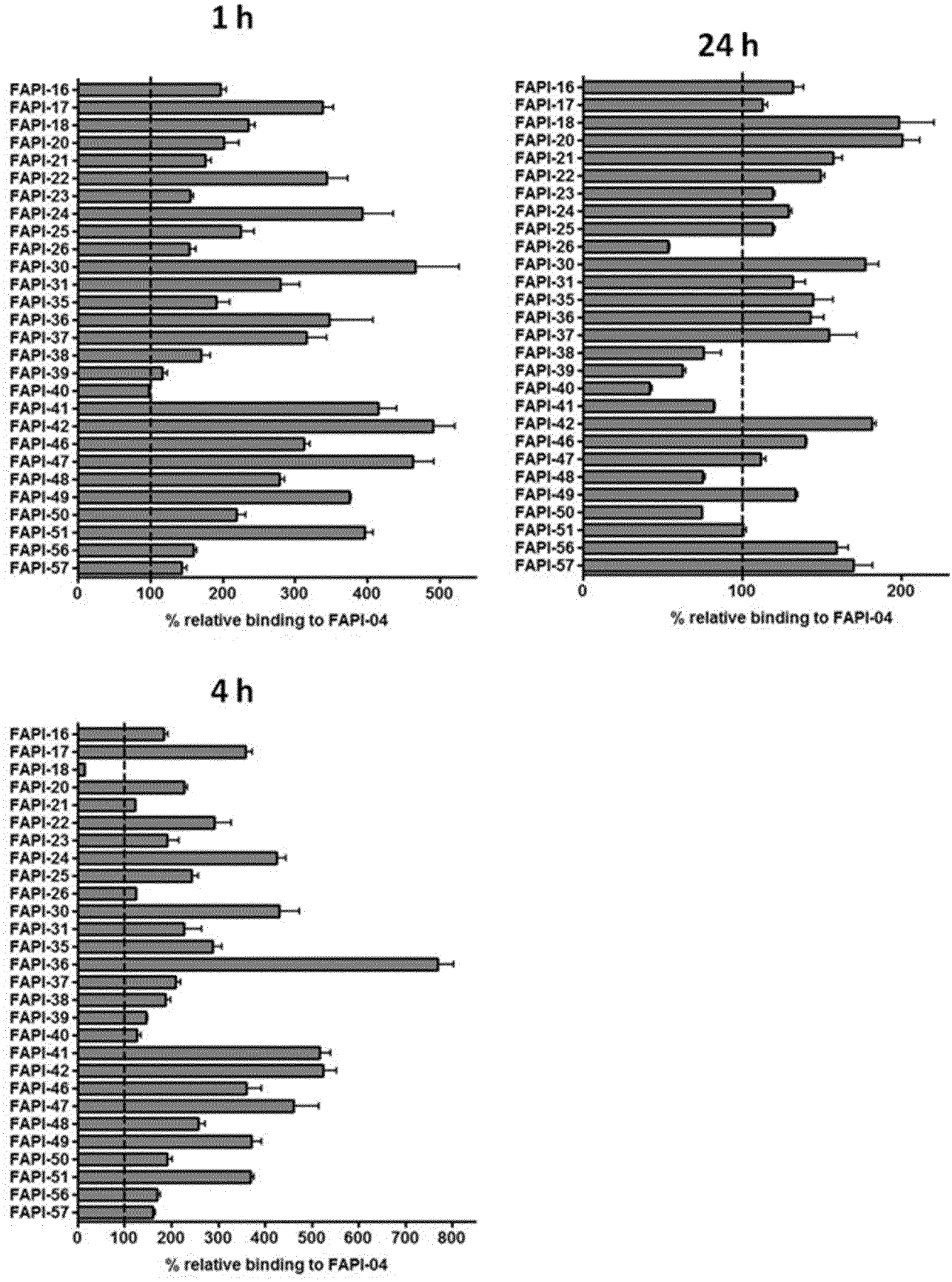

1 h
FAPI-16
FAPI-17
FAPI-18
FAPI-20
FAPI-21
FAPI-22
FAPI-23
FAPI-24
FAPI-25
FAPI-26
FAPI-30
FAPI-31
FAPI-35
FAPI-36
FAPI-37
FAPI-38
FAPI-39
FAPI-40
FAPI-41
FAPI-42
FAPI-46
FAPI-47
FAPI-48
FAPI-49
FAPI-50
FAPI-51
FAPI-56
FAPI-57
0
100
200
300
400
500
% relative binding to FAPI-04
24 h
FAPI-16
FAPI-17
FAPI-18
FAPI-20
FAPI-21
FAPI-22
FAPI-23
FAPI-24
FAPI-25
FAPI-26
FAPI-30
FAPI-31
FAPI-35
FAPI-36
FAPI-37
FAPI-38
FAPI-39
FAPI-40
FAPI-41
FAPI-42
FAPI-46
FAPI-47
FAPI-48
FAPI-49
FAPI-50
FAPI-51
FAPI-56
FAPI-57
0
100
200
% relative binding to FAPI-04
4 h
FAPI-16
FAPI-17
FAPI-18
FAPI-20
FAPI-21
FAPI-22
FAPI-23
FAPI-24
FAPI-25
FAPI-26
FAPI-30
FAPI-31
FAPI-35
FAPI-36
FAPI-37
FAPI-38
FAPI-39
FAPI-40
FAPI-41
FAPI-42
FAPI-46
FAPI-47
FAPI-48
FAPI-49
FAPI-50
FAPI-51
FAPI-56
FAPI-57
0
100
200
300
400
500
600
700
800
% relative binding to FAPI-04

Figure 17

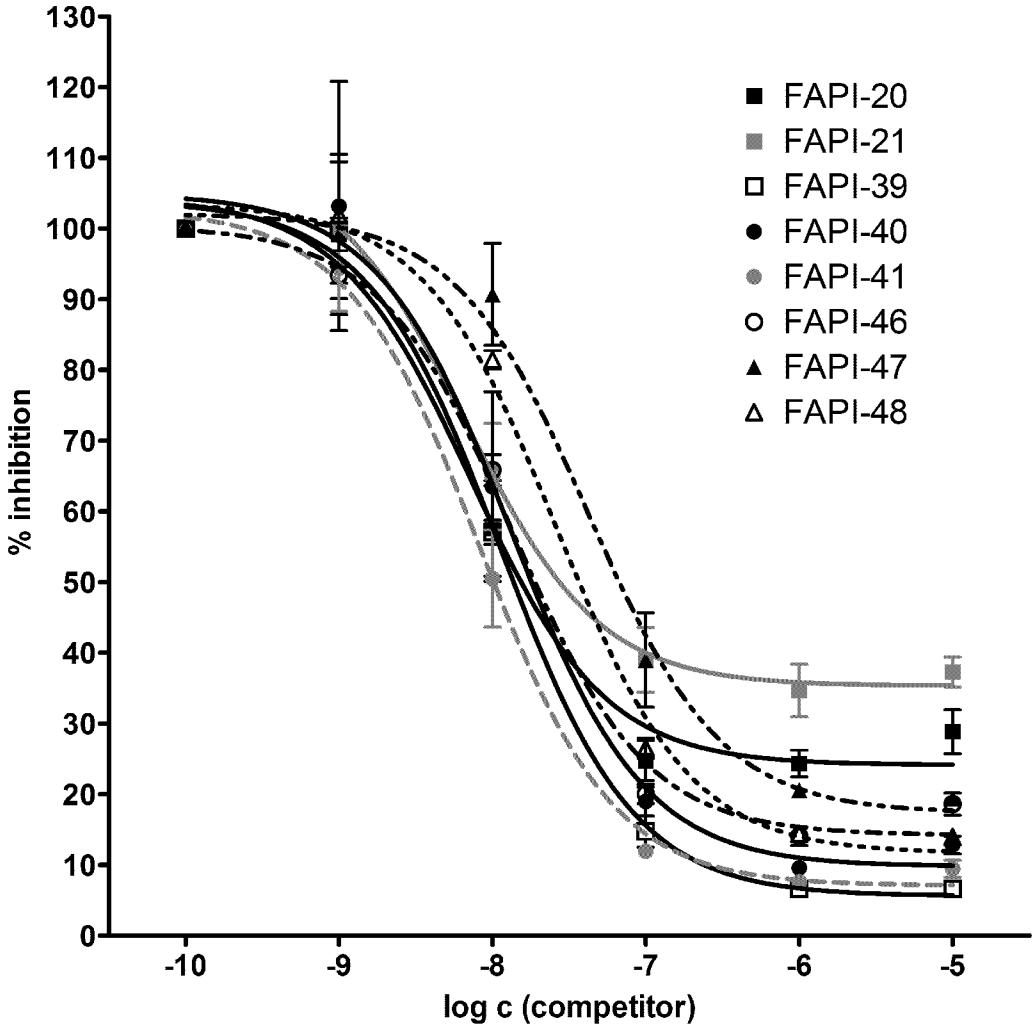

130
120
110
100
90
80
70
60
50
40
30
20
10
0
% inhibition
-10
-9
-8
-7
-6
-5
log c (competitor)
FAPI-20
FAPI-21
FAPI-39
FAPI-40
FAPI-41
FAPI-46
FAPI-47
FAPI-48

Figure 18

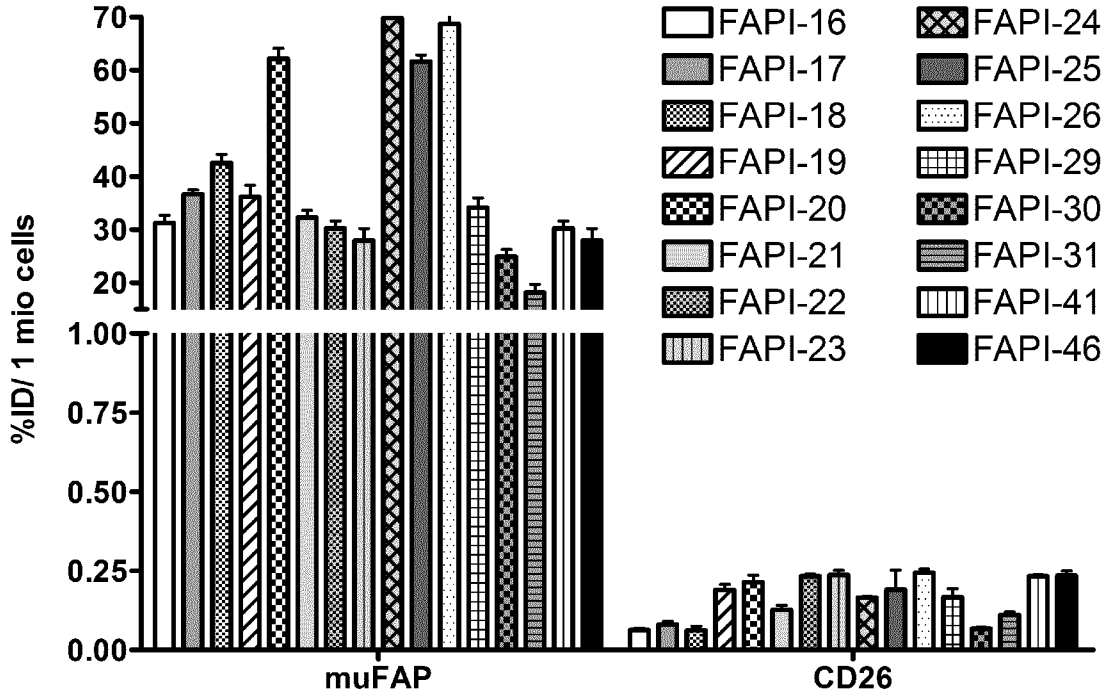
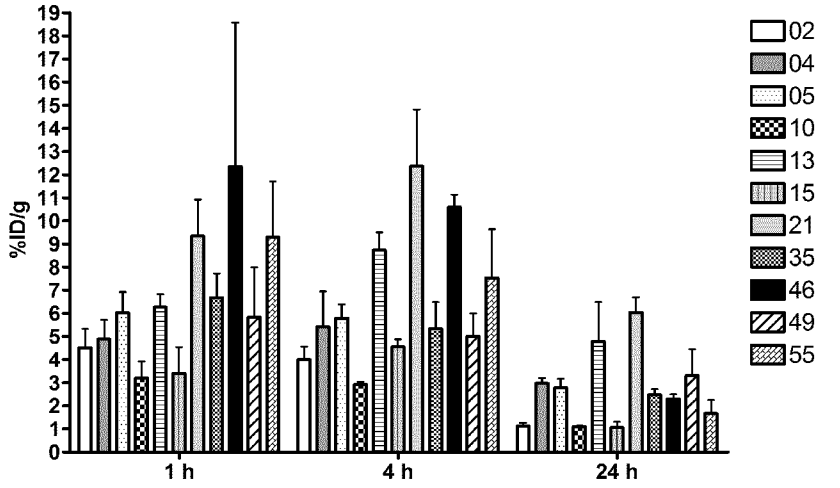
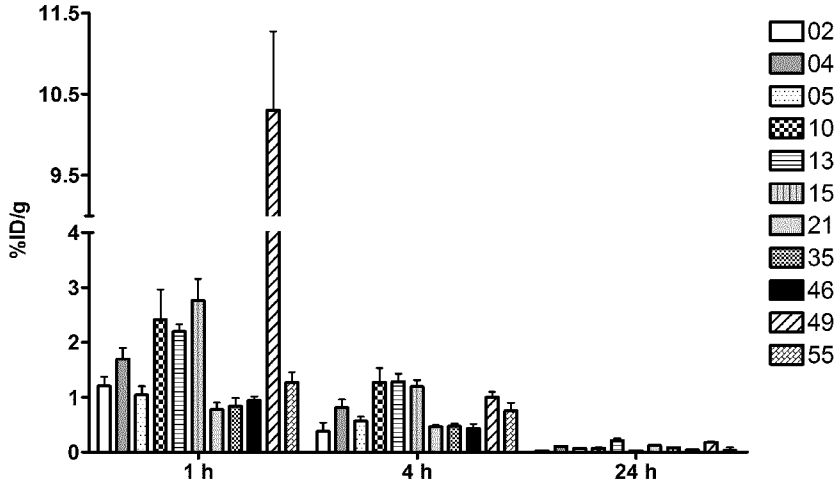

%ID/ 1 mio cells
70
60
50
40
30
20
1.00
0.75
0.50
0.25
0.00
muFAP
CD26
FAPI-16
FAPI-17
FAPI-18
FAPI-19
FAPI-20
FAPI-21
FAPI-22
FAPI-23
FAPI-24
FAPI-25
FAPI-26
FAPI-29
FAPI-30
FAPI-31
FAPI-41
FAPI-46

Figure 19

Tumor



Blood



Kidneys

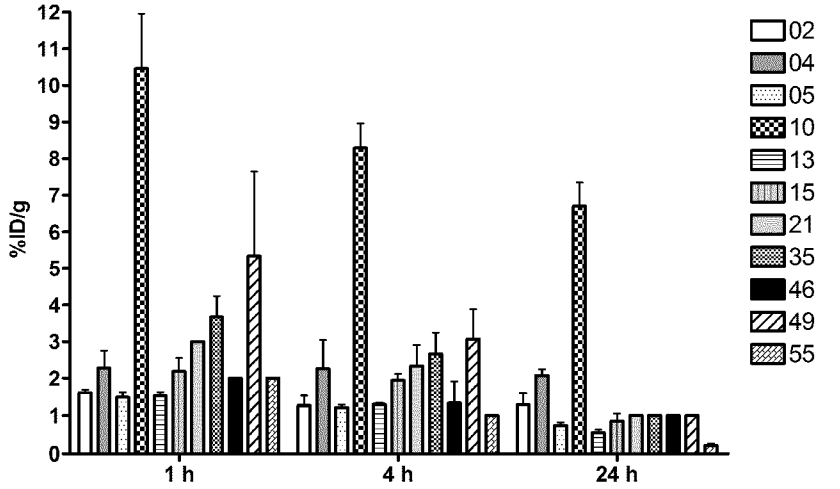


Figure 20

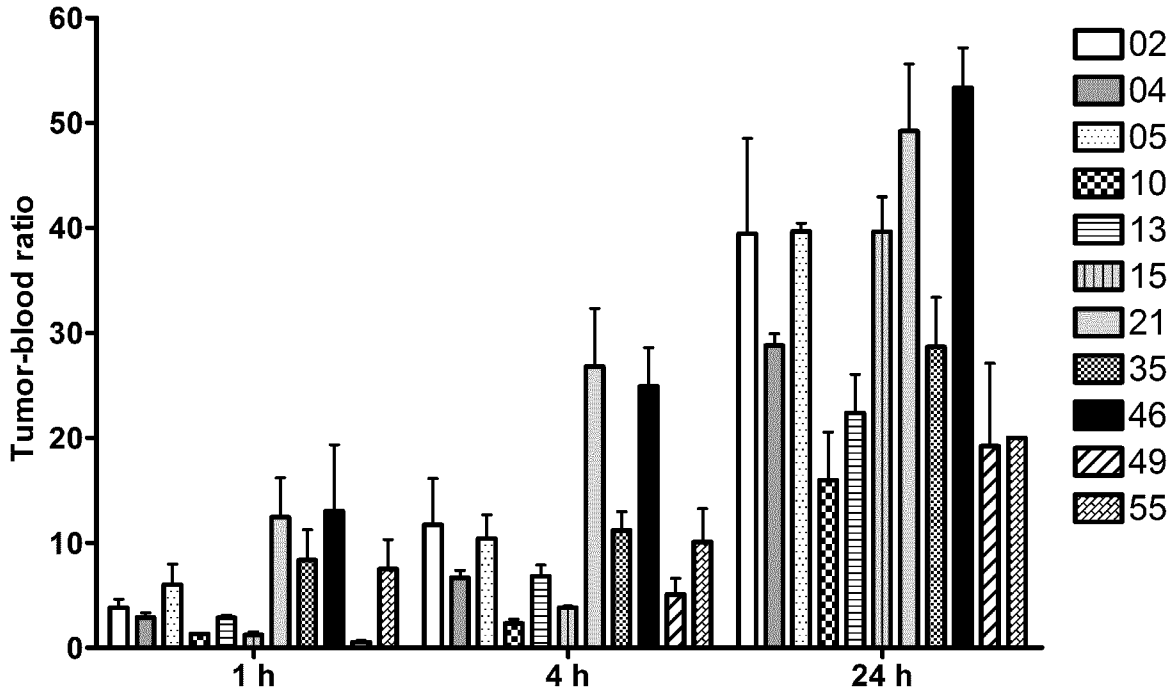


Figure 21

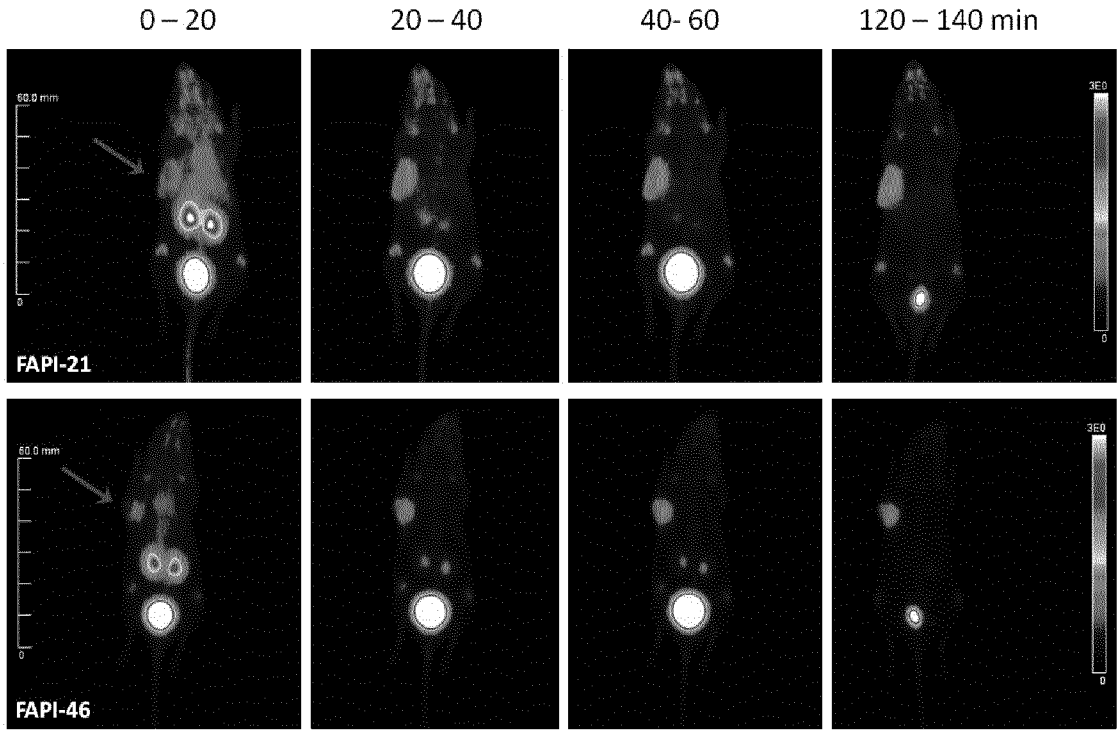


Figure 22

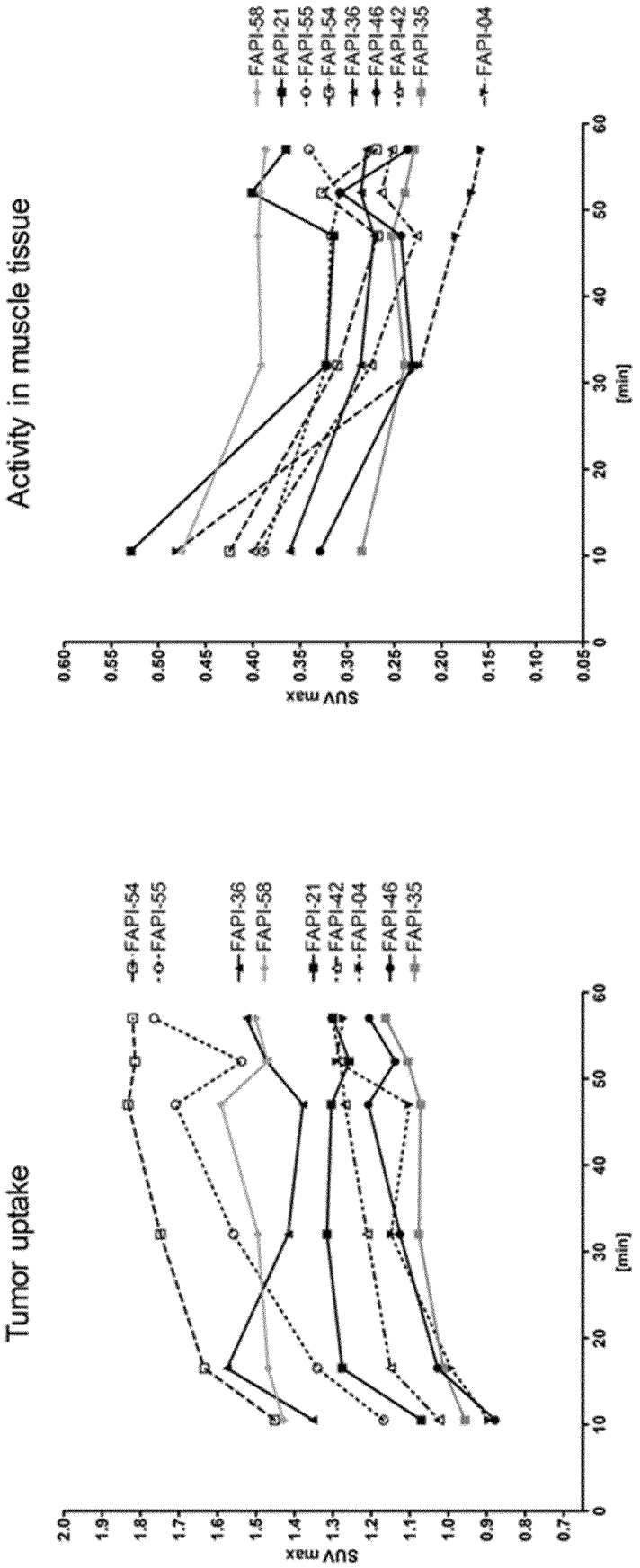
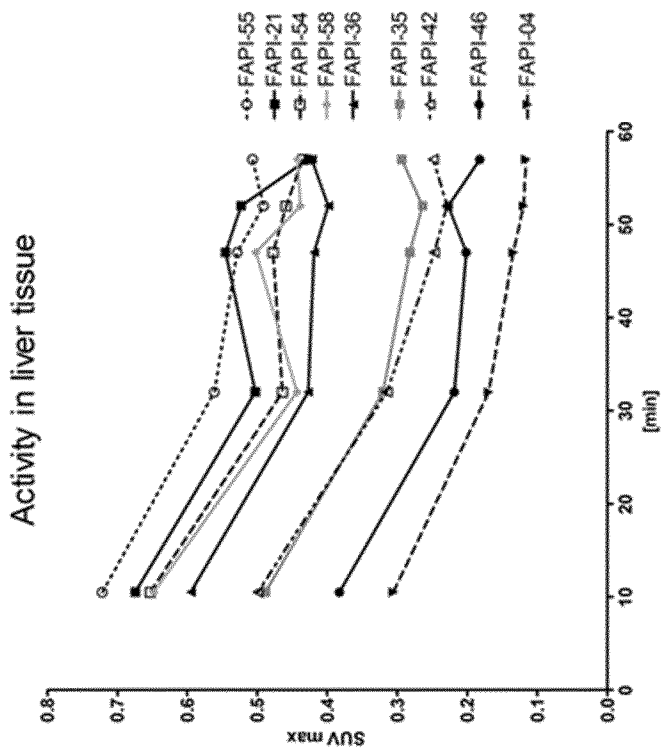

Activity in muscle tissue
SUV max
[min]
FAPI-58
FAPI-21
FAPI-55
FAPI-54
FAPI-36
FAPI-46
FAPI-42
FAPI-35
FAPI-04
Tumor uptake
SUV max
[min]
FAPI-54
FAPI-55
FAPI-36
FAPI-58
FAPI-21
FAPI-42
FAPI-04
FAPI-46
FAPI-35

Figure 22 continued



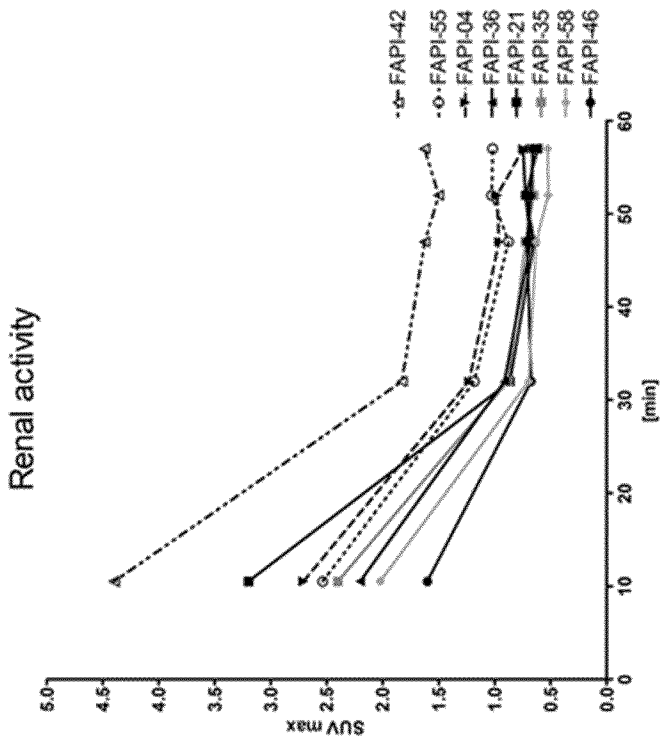


Figure 23

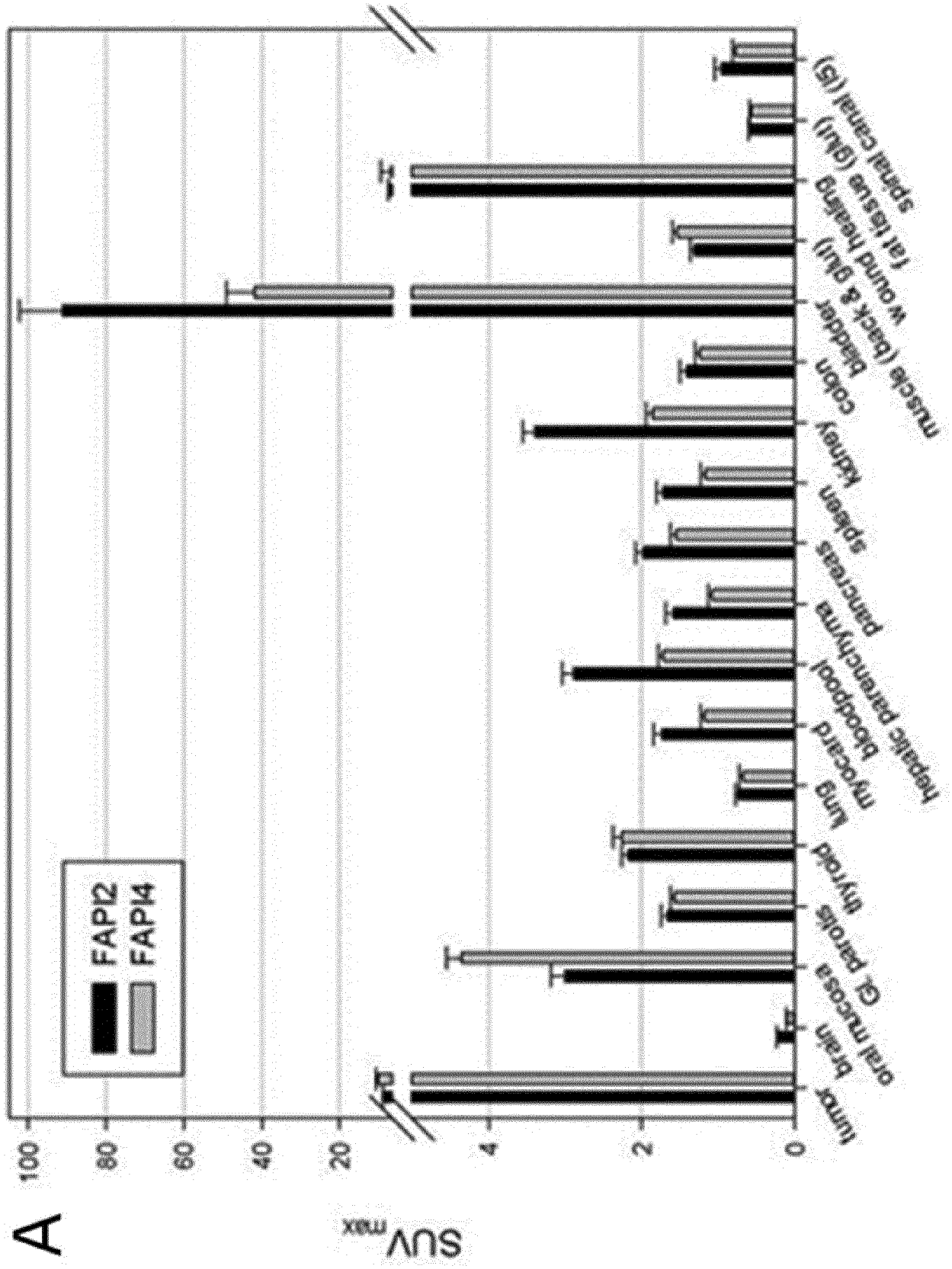

A
SUV max
FAPI2
FAPI4
tumor
brain
oral mucosa
GI patolis
thyroid
lung
myocard
bloodpool
hepatic parenchyma
pancreas
spleen
kidney
colon
bladder
muscle (back & glut)
wound healing
fat tissue (glut)
spinal canal (ls)

Figure 23 continued

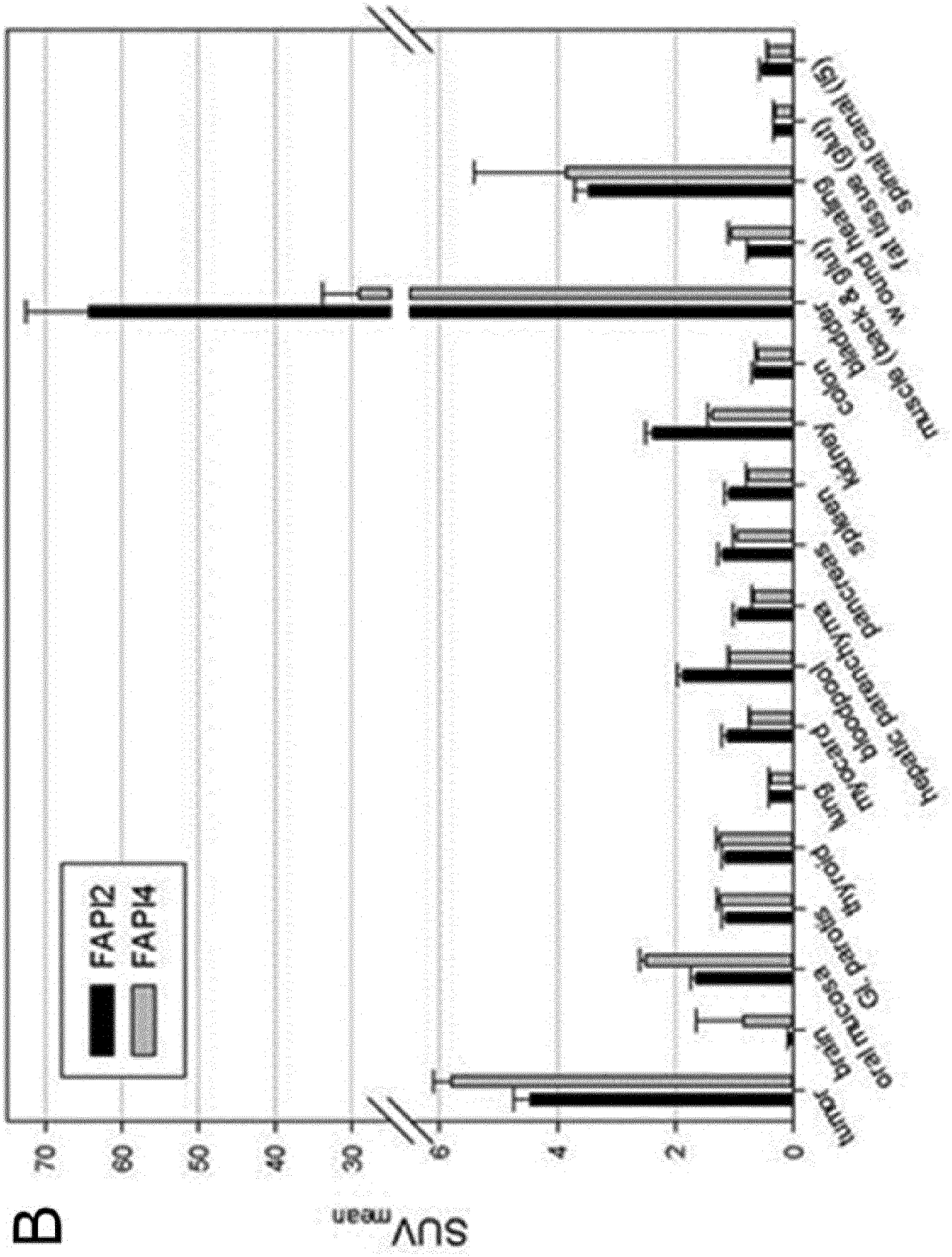


Figure 24

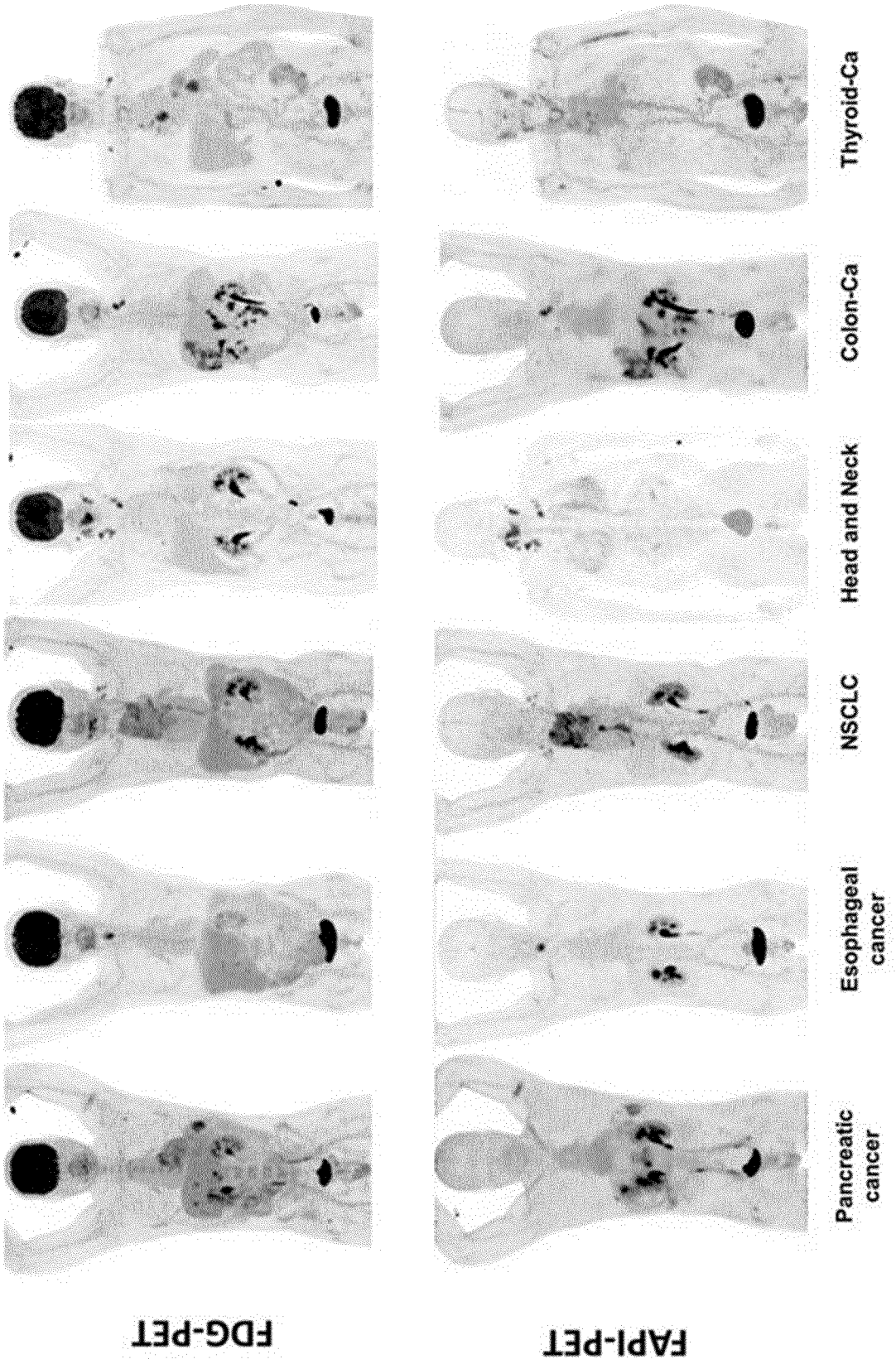

FDG-PET
FAPI-PET
Thyroid-Ca
Colon-Ca
Head and Neck
NSCLC
Esophageal cancer
Pancreatic cancer

Figure 24 continued

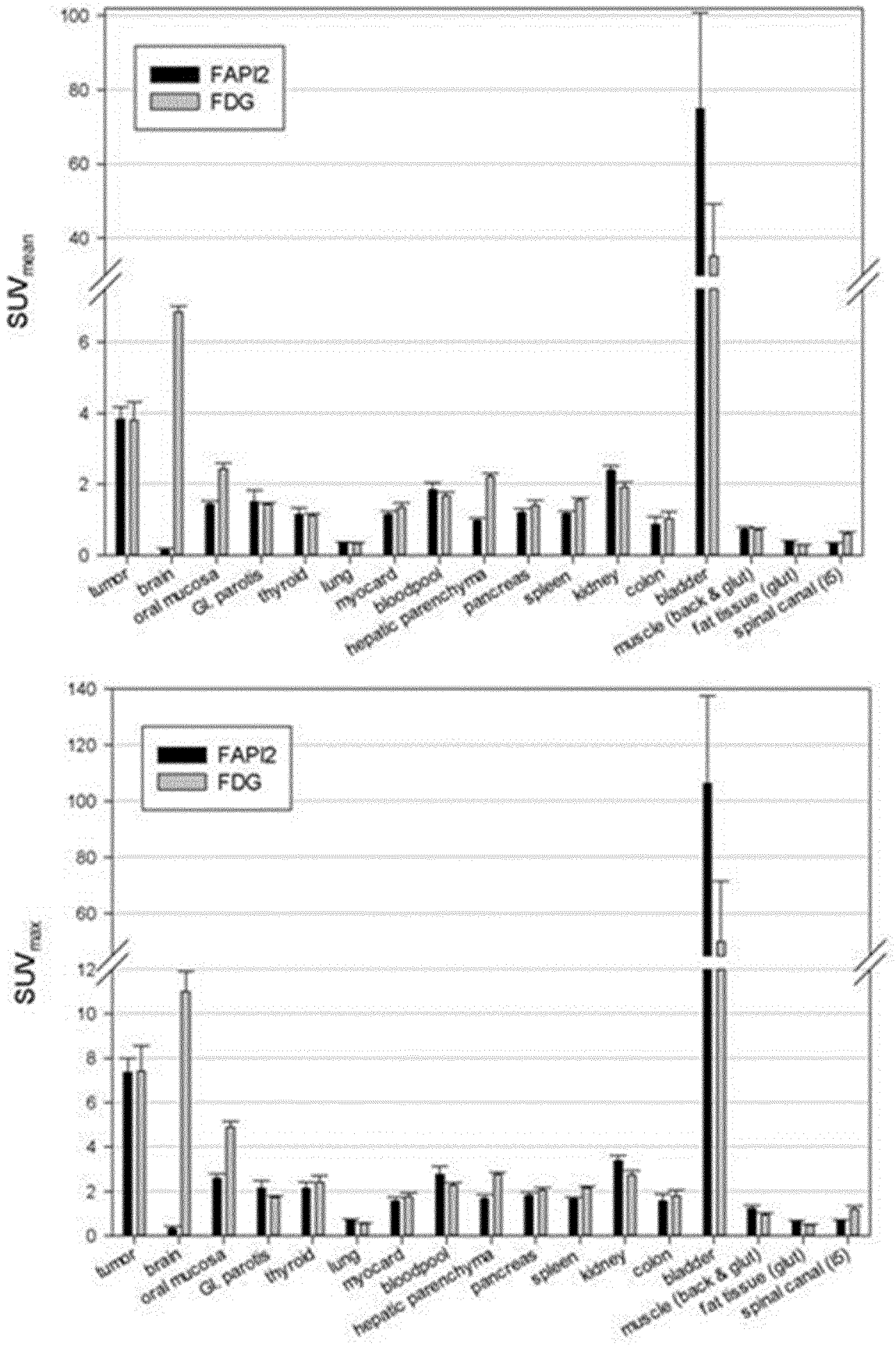


Figure 25

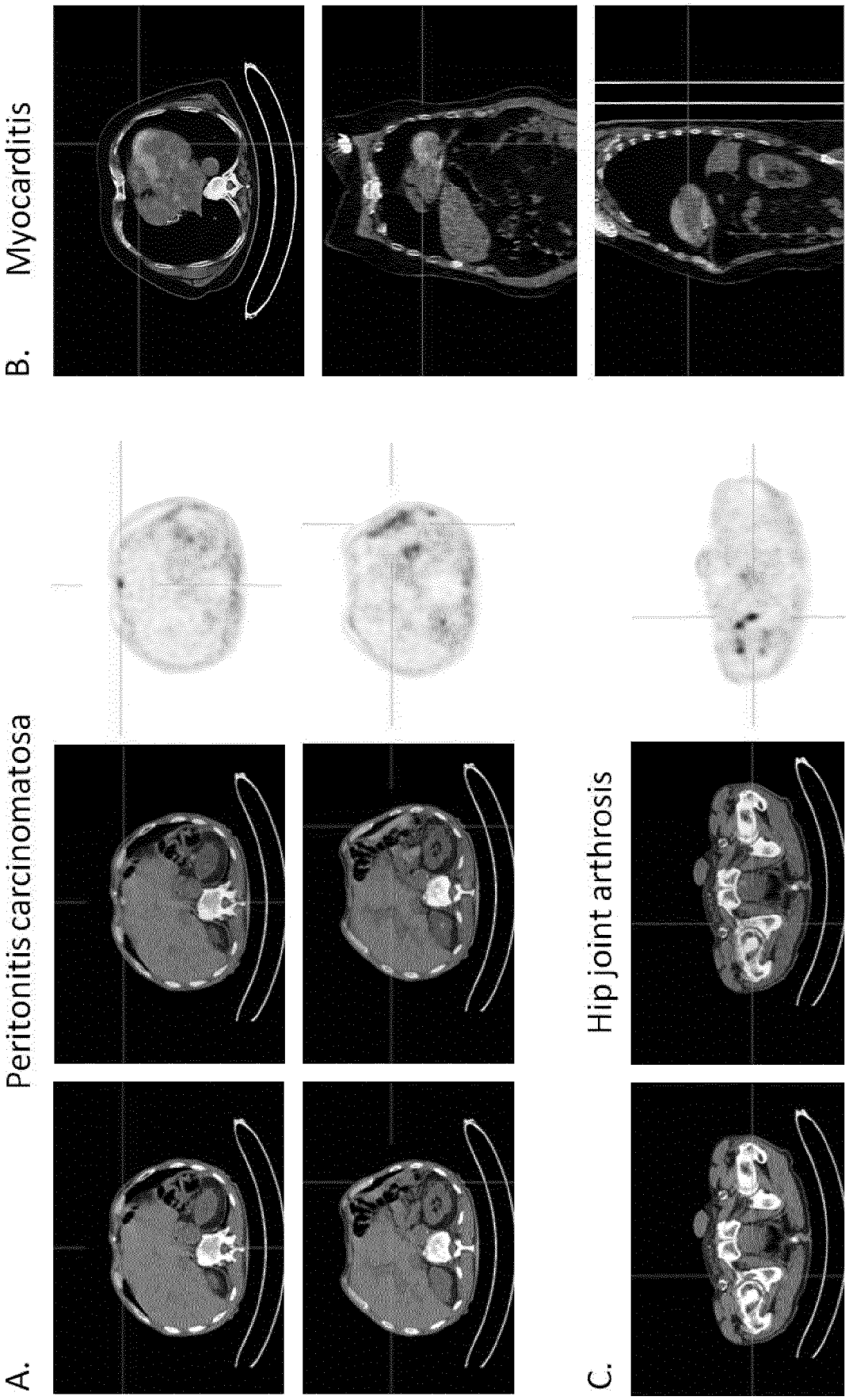

A.
Peritonitis carcinomatosa
B.
Myocarditis
C.
Hip joint arthrosis

Figure 26

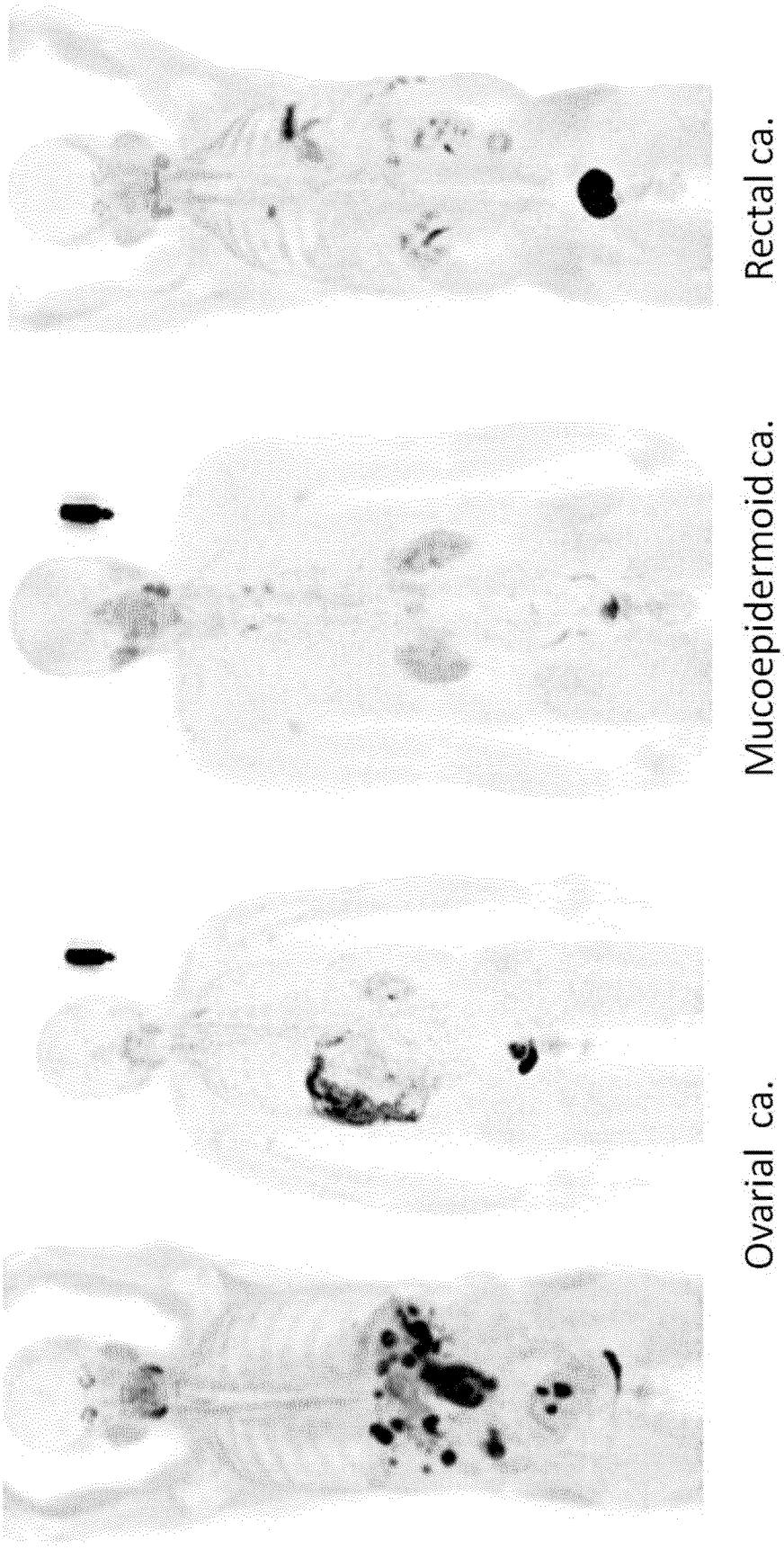


Figure 27

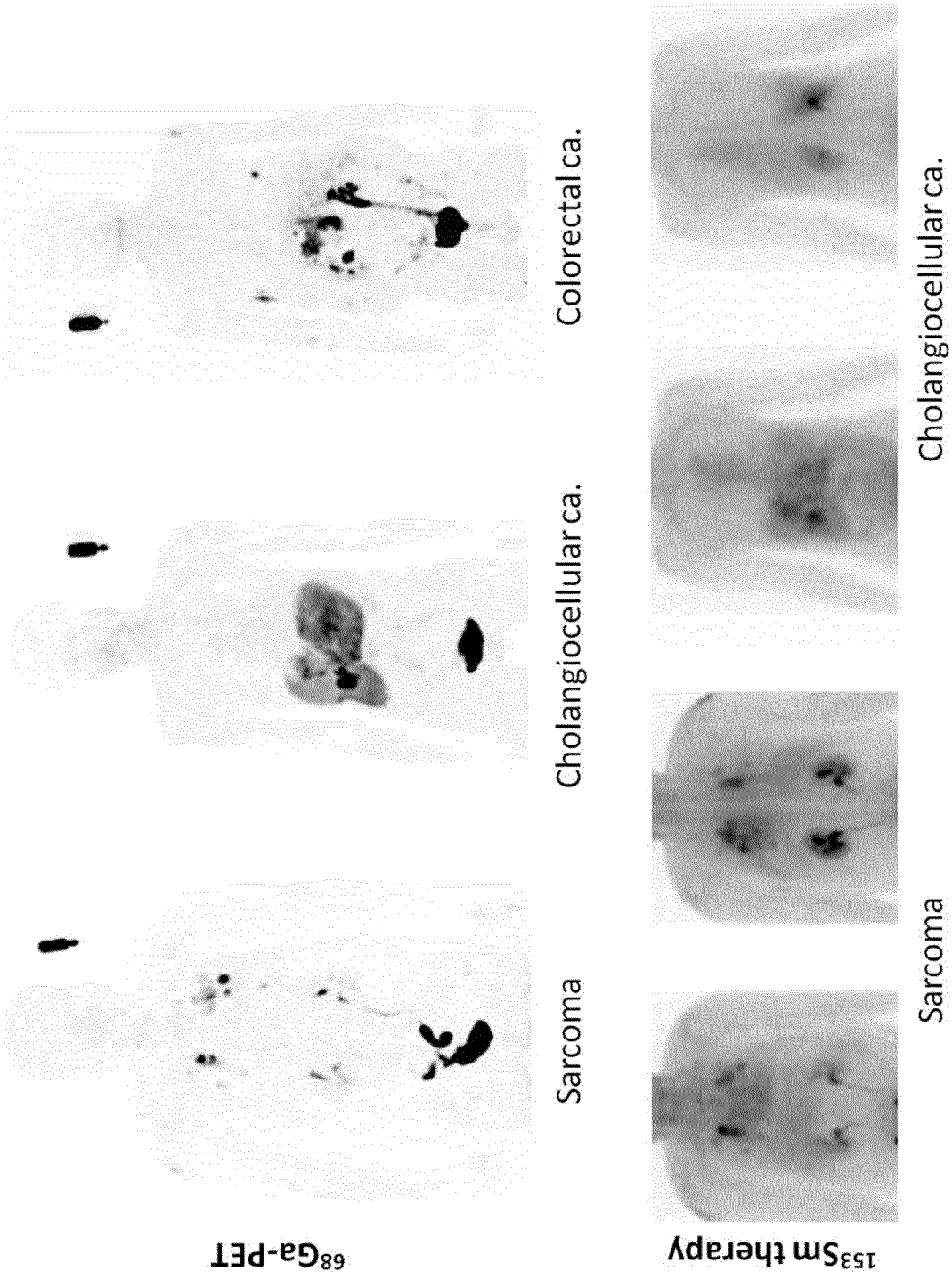

68Ga-PET
153Sm therapy
Sarcoma
Cholangiocellular ca.
Colorectal ca.
Sarcoma
Cholangiocellular ca.

Figure 28

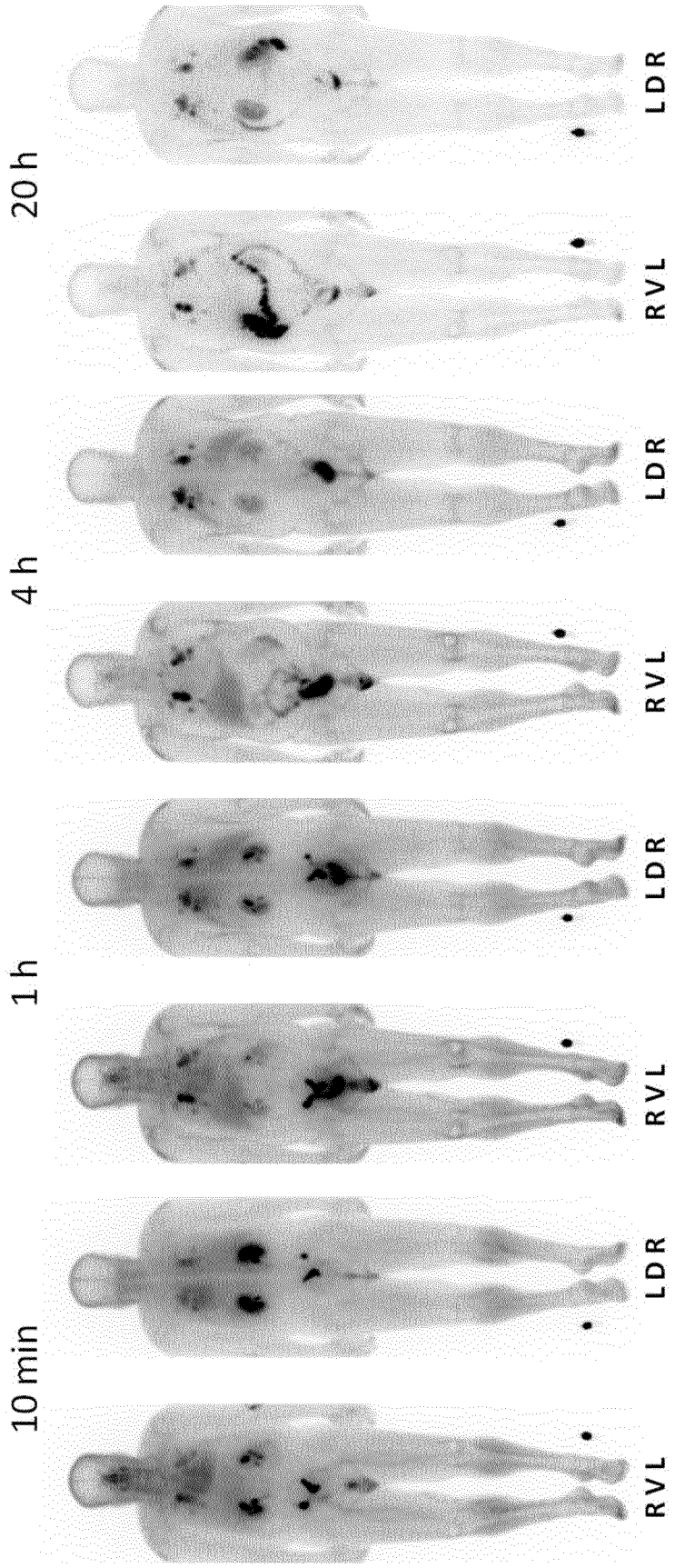


Figure 29

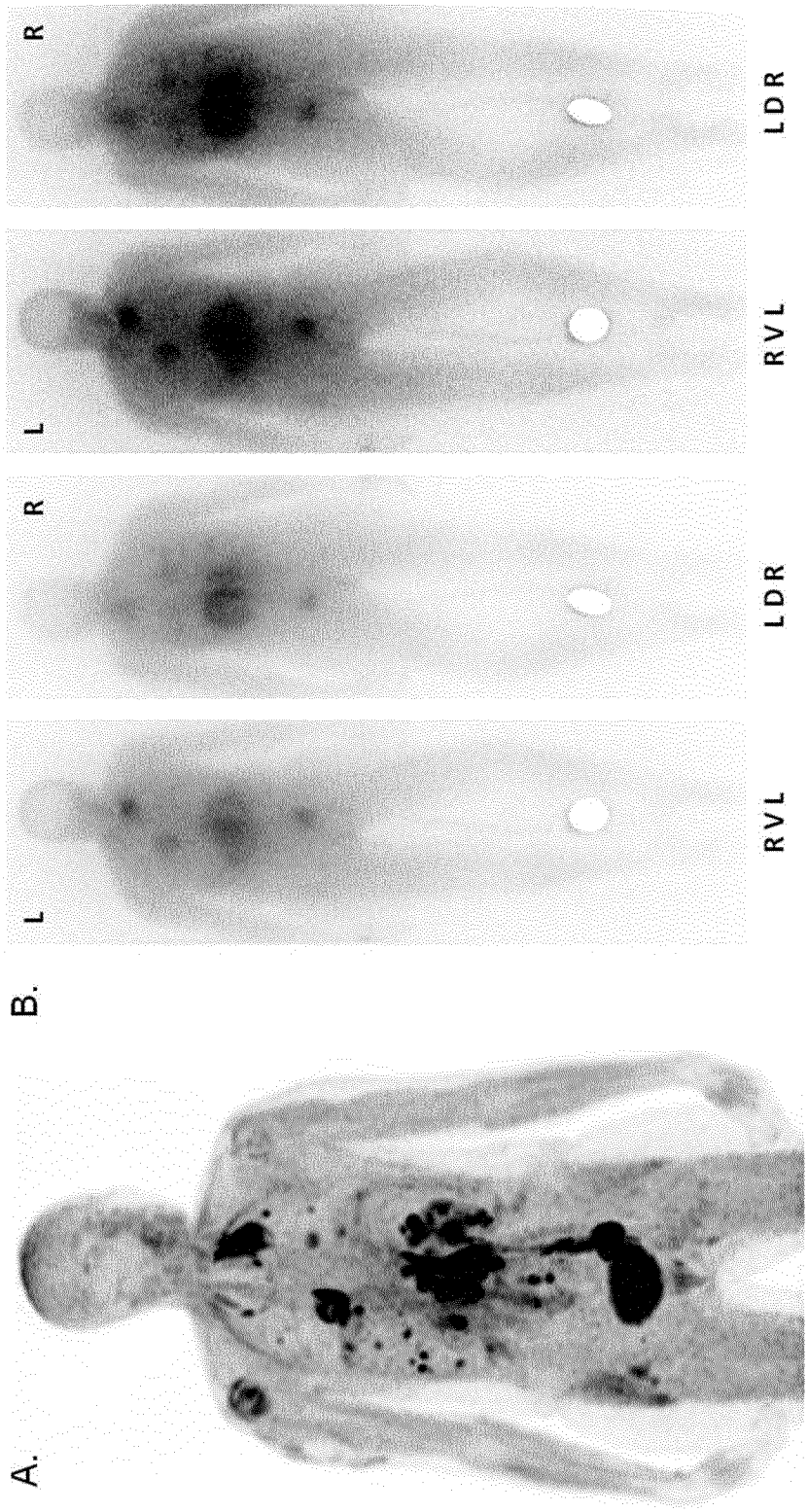


Figure 30

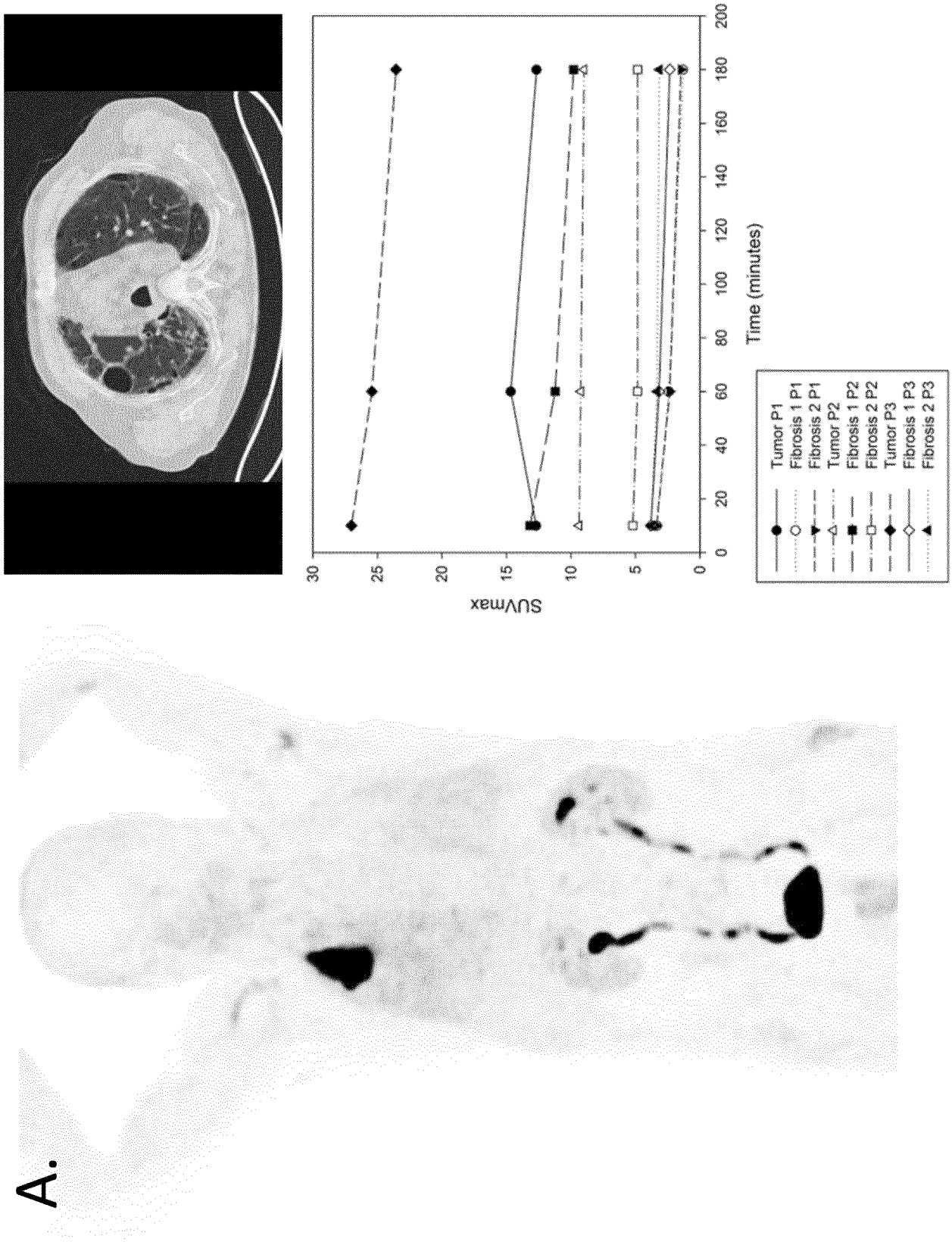
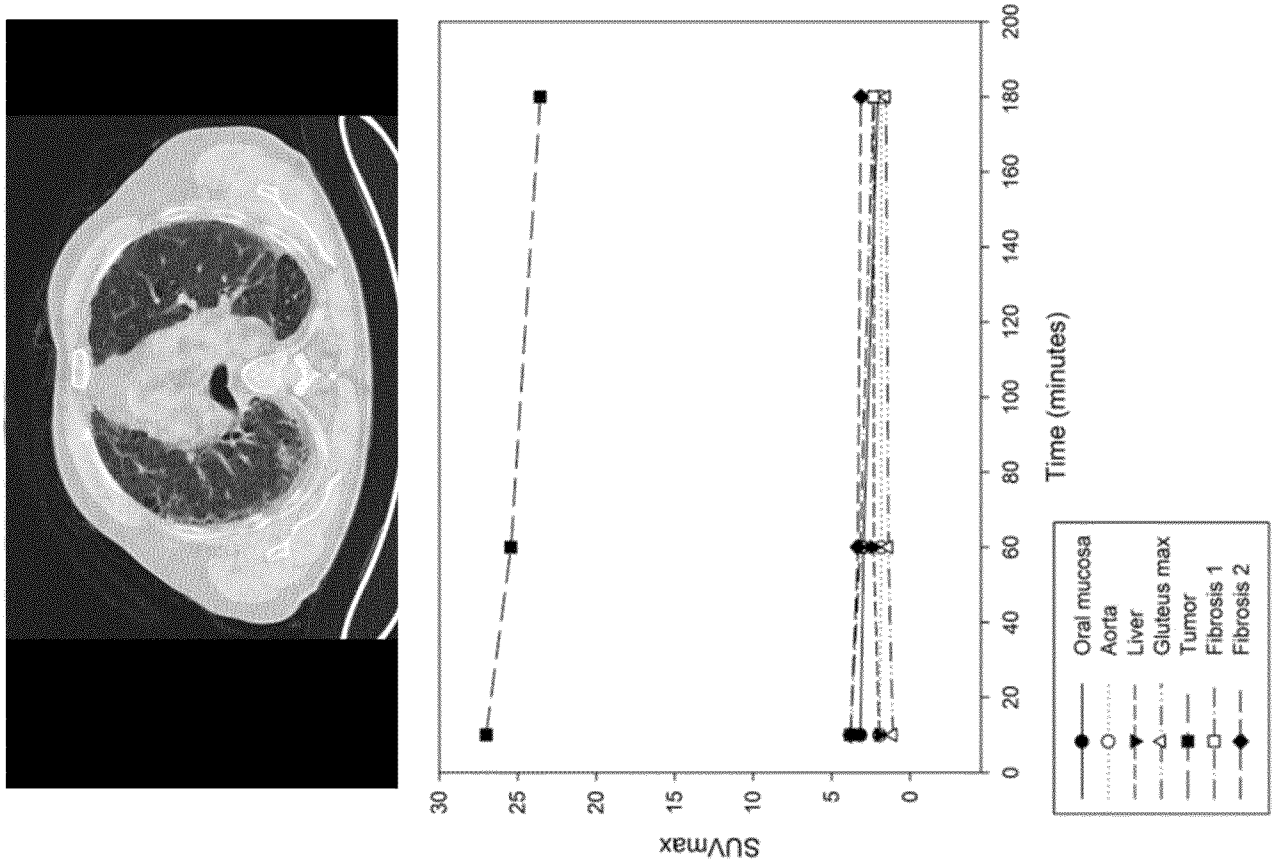

A.
SUVmax
Time (minutes)
Tumor P1
Fibrosis 1 P1
Fibrosis 2 P1
Tumor P2
Fibrosis 1 P2
Fibrosis 2 P2
Tumor P3
Fibrosis 1 P3
Fibrosis 2 P3

Figure 30 continued



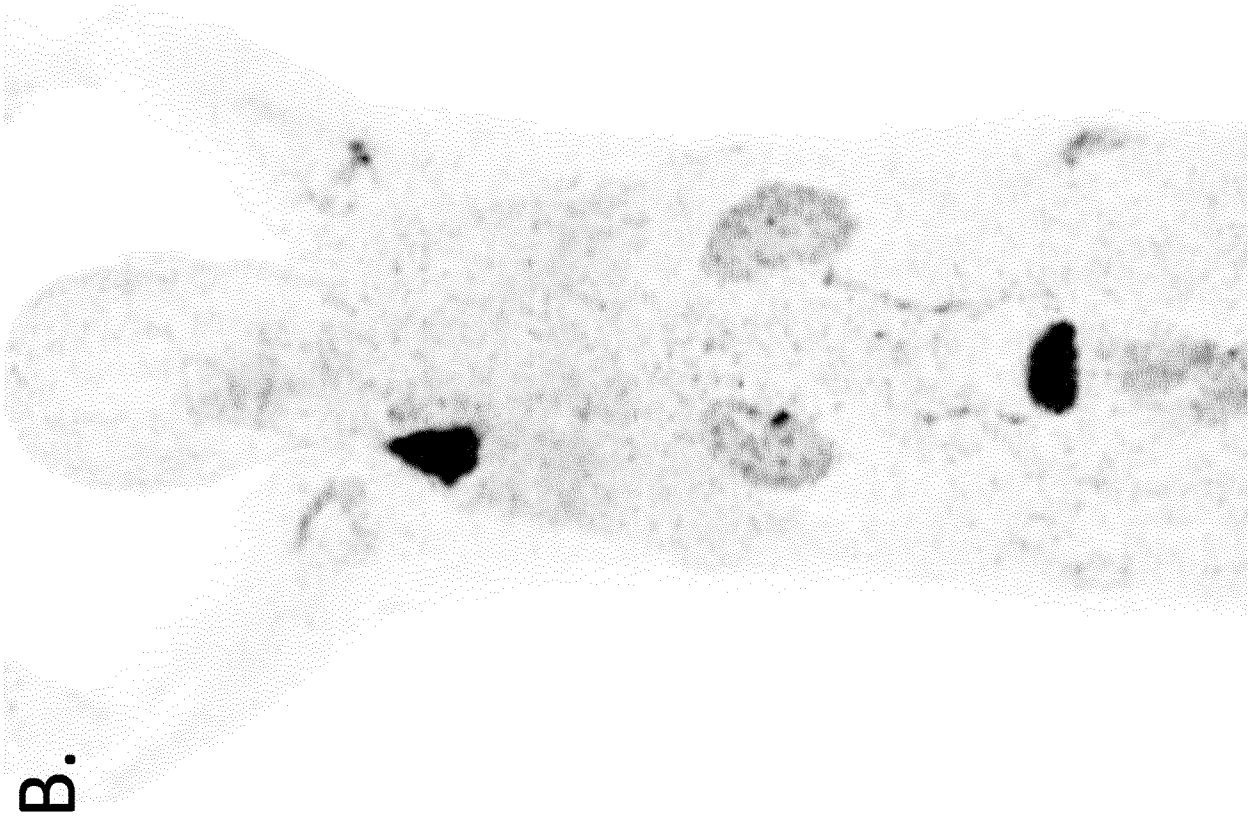
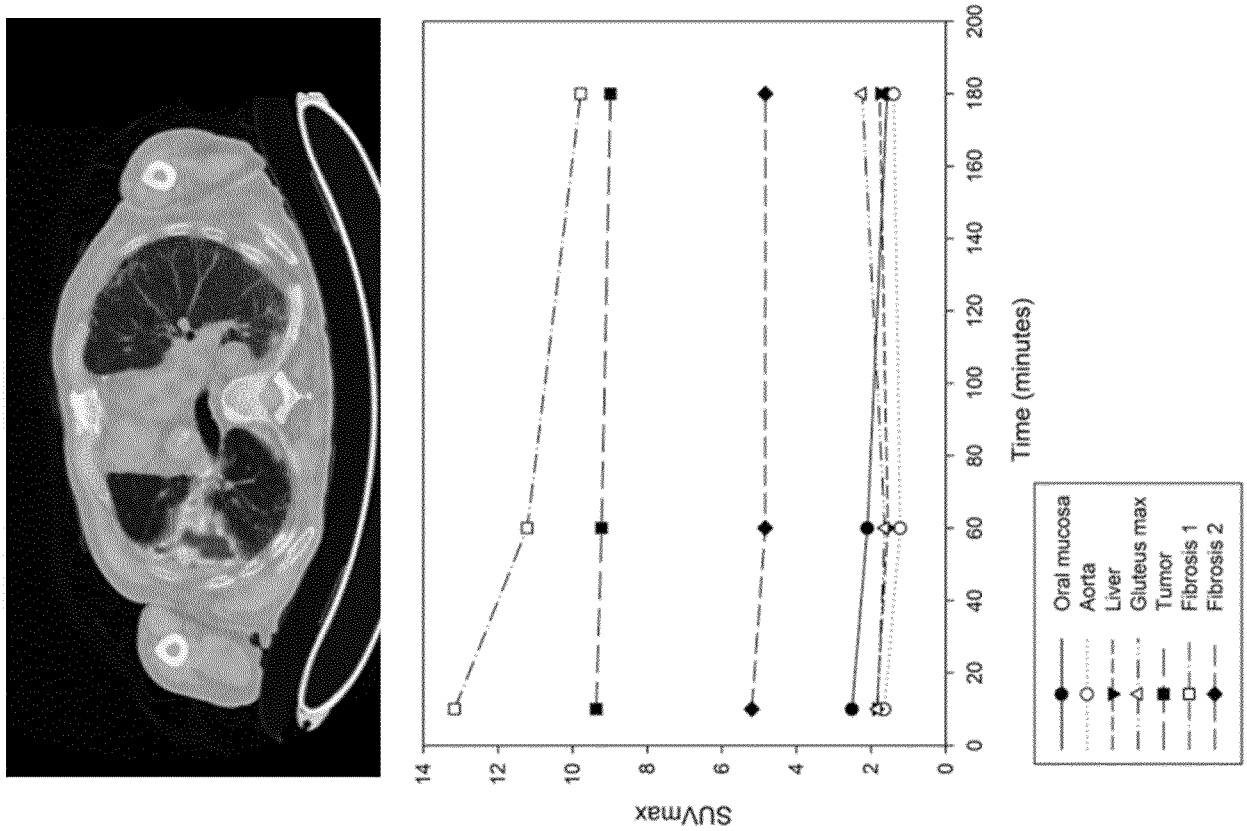
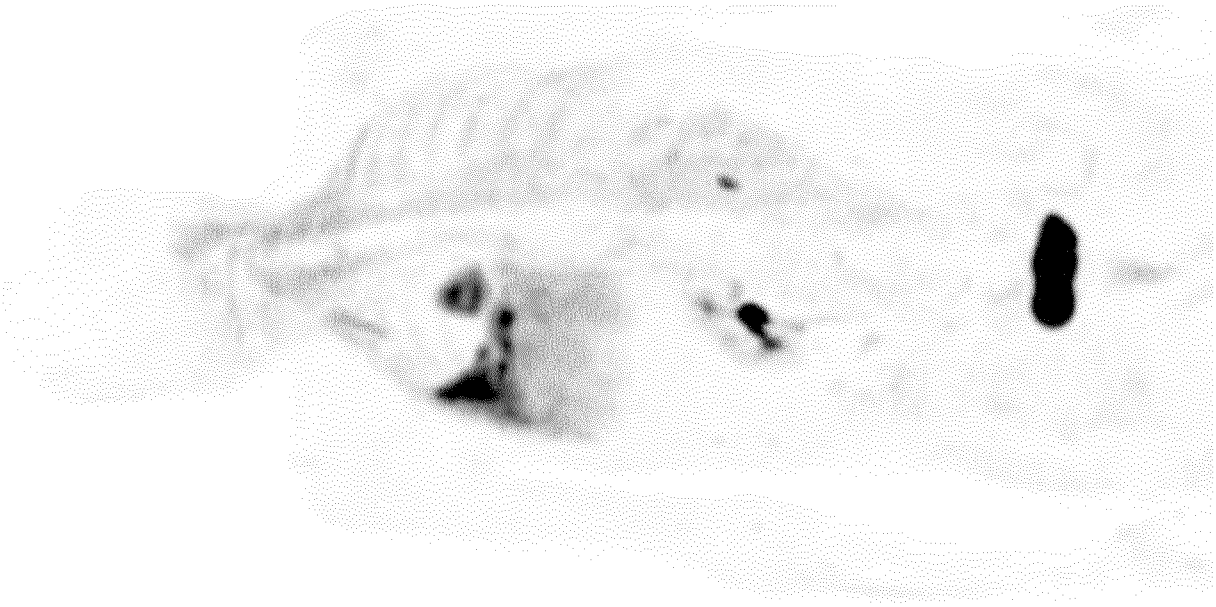


Figure 30 continued





ن

Figure 31

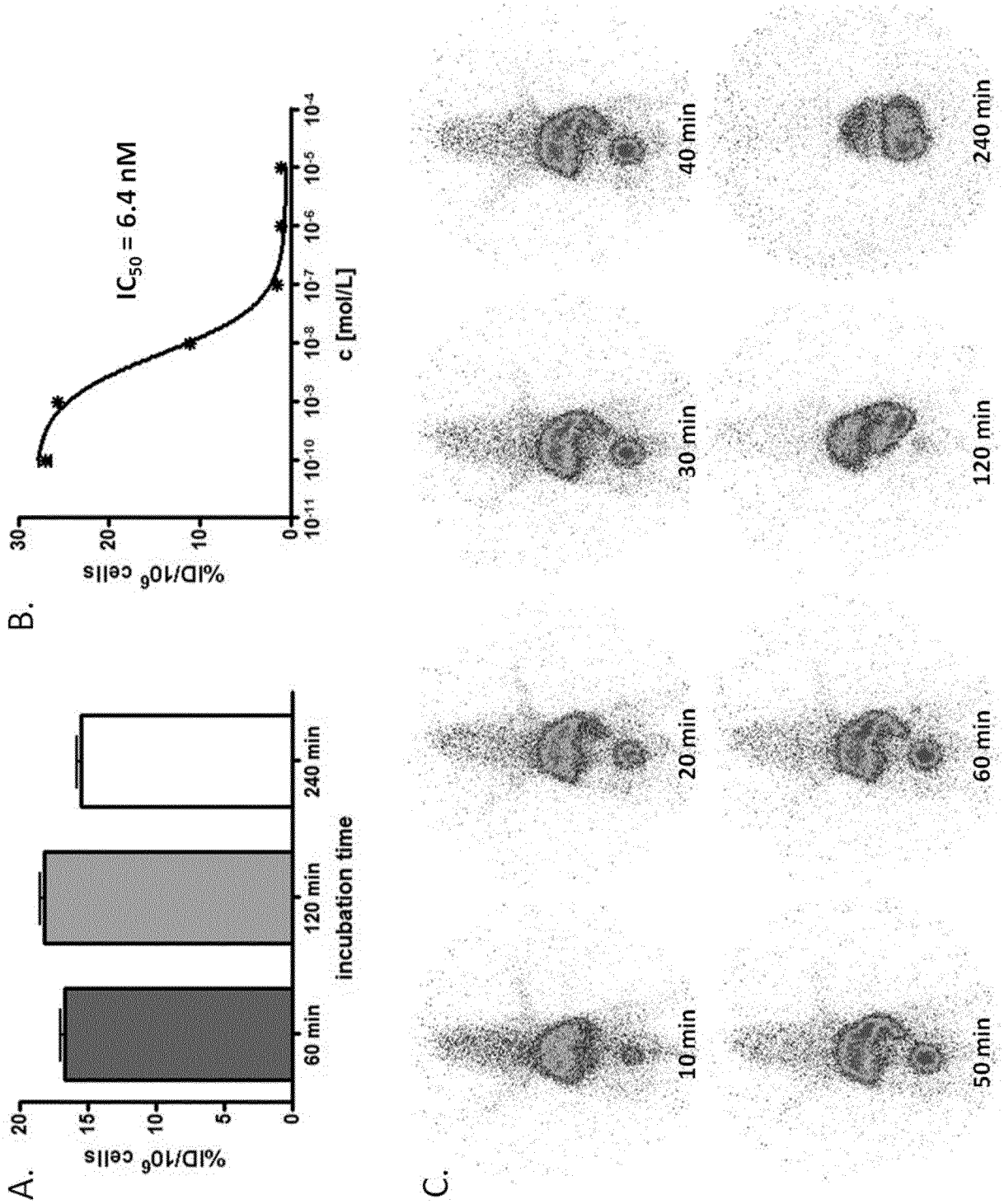

A.
%ID/10^6 cells
incubation time
60 min
120 min
240 min
B.
IC50 = 6.4 nM
%ID/10^6 cells
c [mol/L]
C.
10 min
20 min
30 min
40 min
50 min
60 min
120 min
240 min

Figure 32

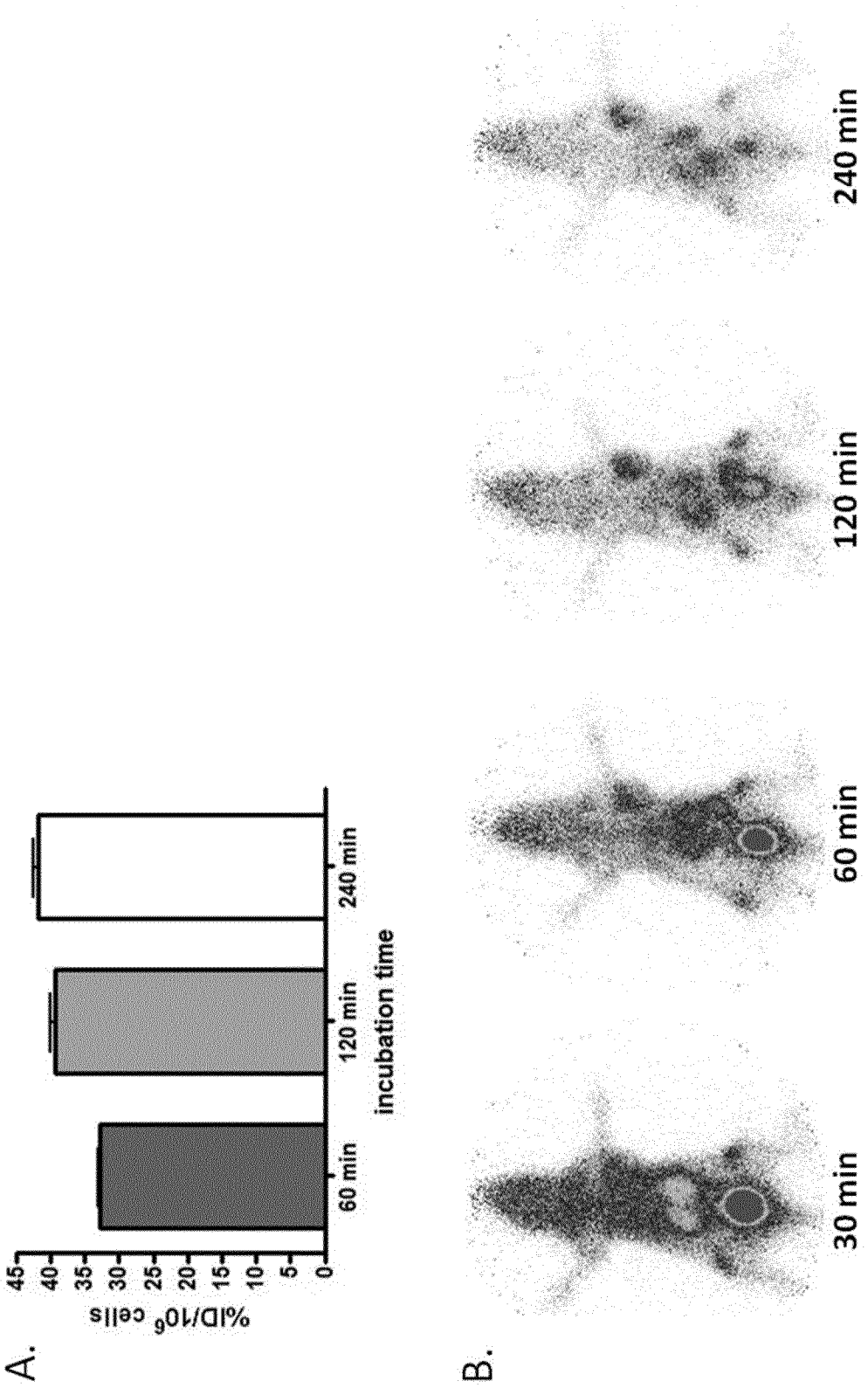

A.
%ID/10^6 cells
45
40
35
30
25
20
15
10
5
0
60 min
120 min
240 min
incubation time
B.
30 min
60 min
120 min
240 min

Figure 33

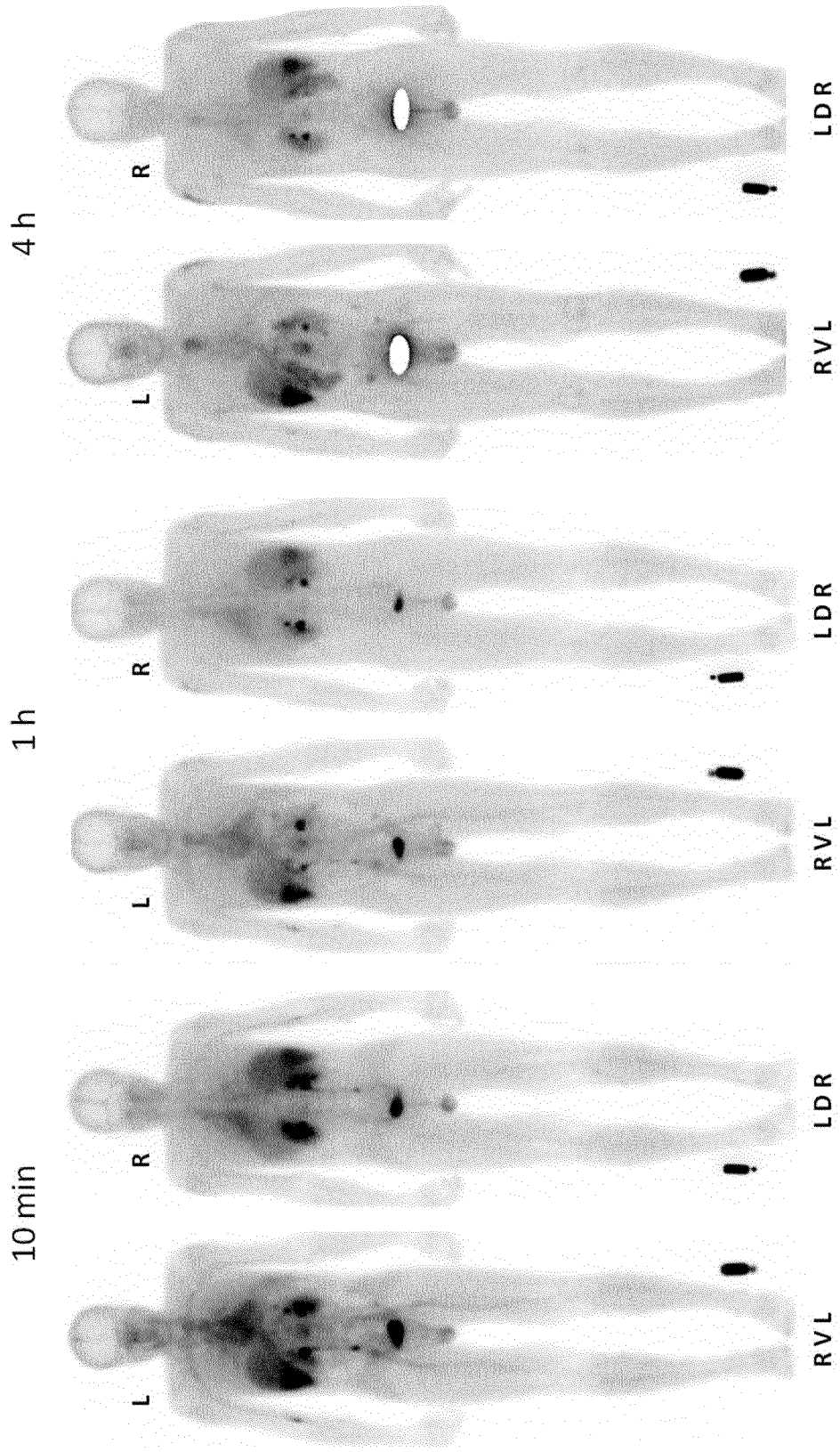


Figure 34

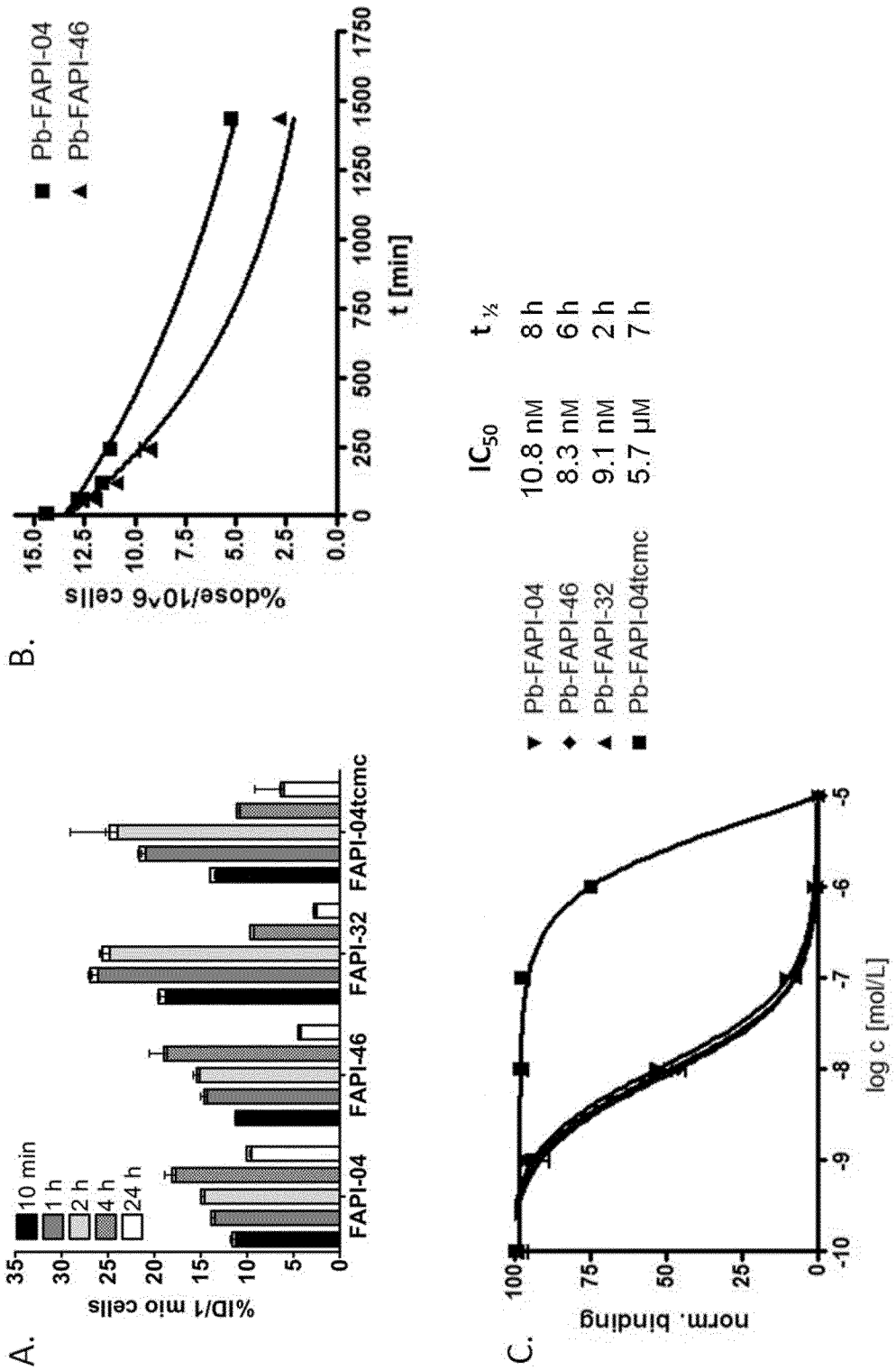

A.
%ID/1 mio cells
10 min
1 h
2 h
4 h
24 h
FAPI-04
FAPI-46
FAPI-32
FAPI-04tcmc
B.
%dose/10^6 cells
t [min]
Pb-FAPI-04
Pb-FAPI-46
C.
norm. binding
log c [mol/L]
IC50
t ½
Pb-FAPI-04 10.8 nM 8 h
Pb-FAPI-46 8.3 nM 6 h
Pb-FAPI-32 9.1 nM 2 h
Pb-FAPI-04tcmc 5.7 µM 7 h

Figure 35

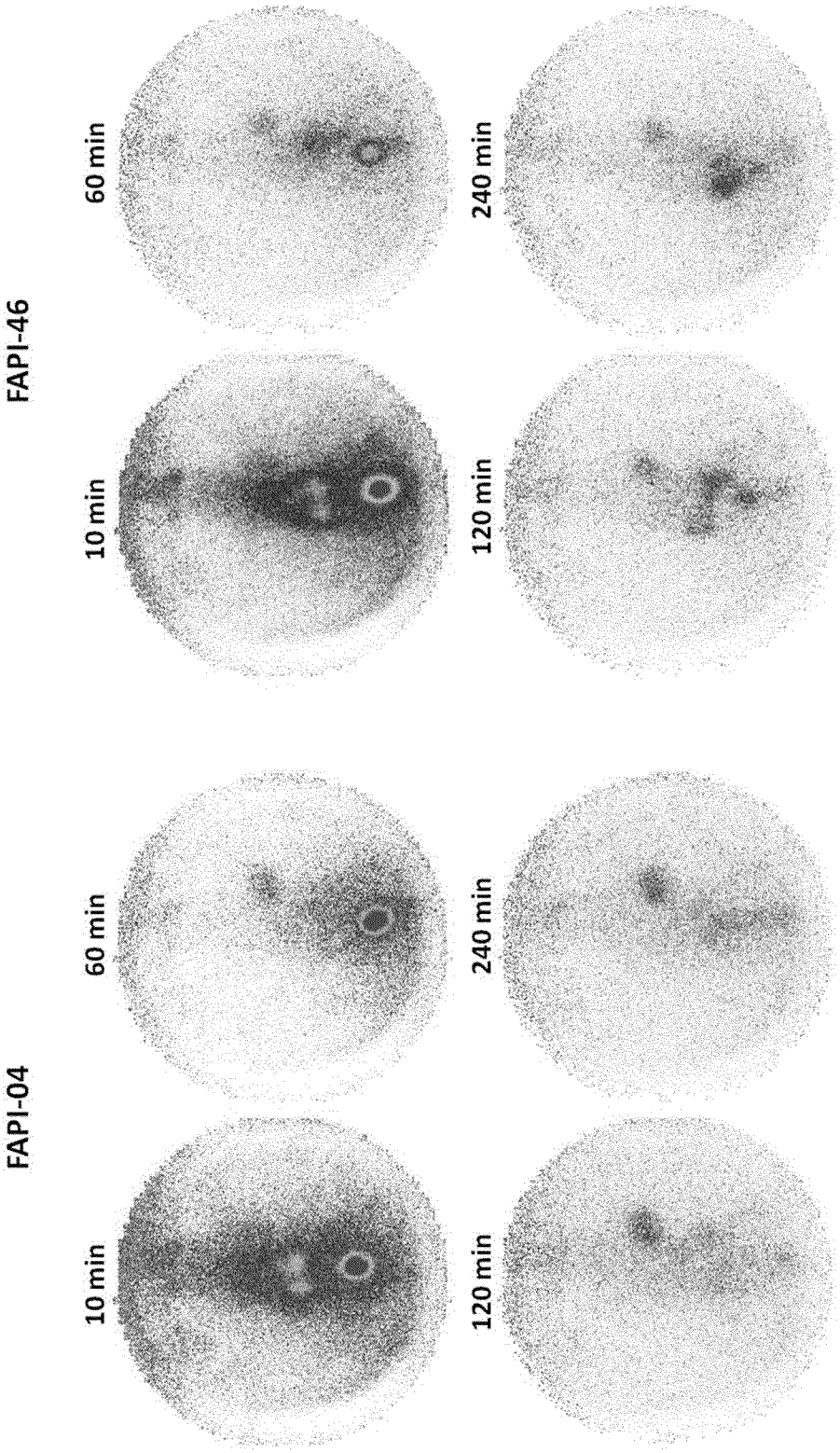

FAPI-46
60 min
240 min
10 min
120 min
FAPI-04
60 min
240 min
10 min
120 min

Figure 36

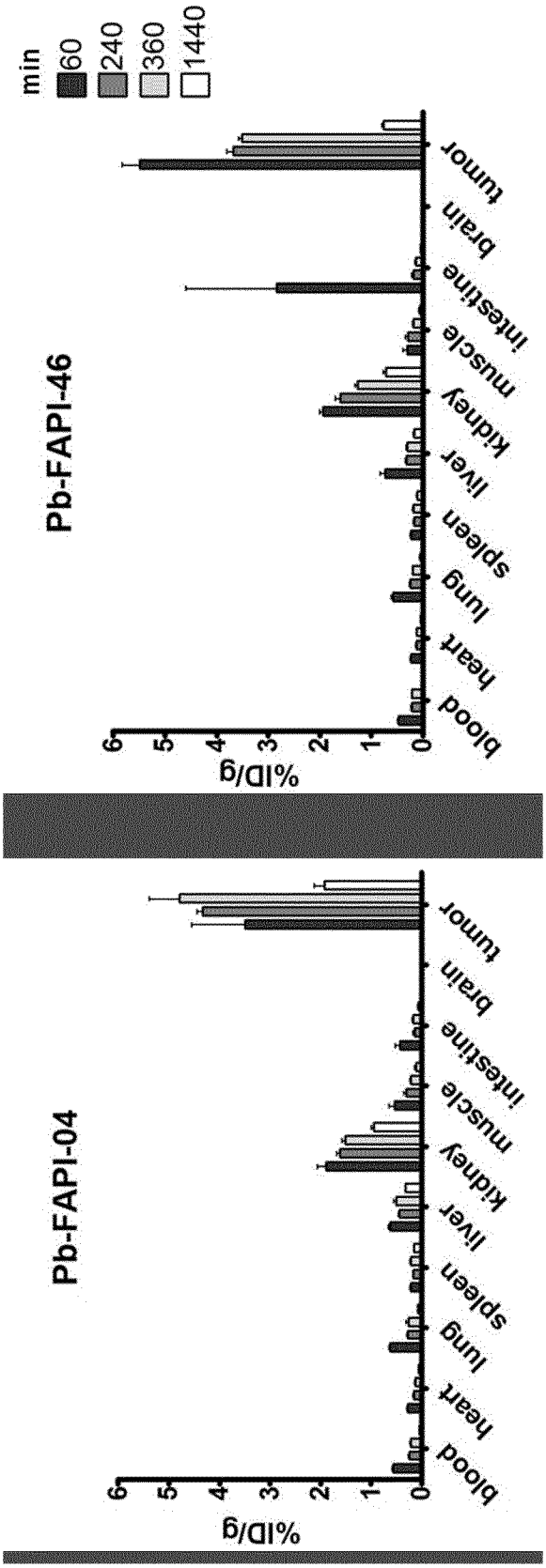

min
60
240
360
1440
Pb-FAPI-46
%ID/g
0
1
2
3
4
5
6
blood
heart
lung
spleen
liver
kidney
muscle
intestine
brain
tumor
Pb-FAPI-04
%ID/g
0
1
2
3
4
5
6
blood
heart
lung
spleen
liver
kidney
muscle
intestine
brain
tumor

Figure 37

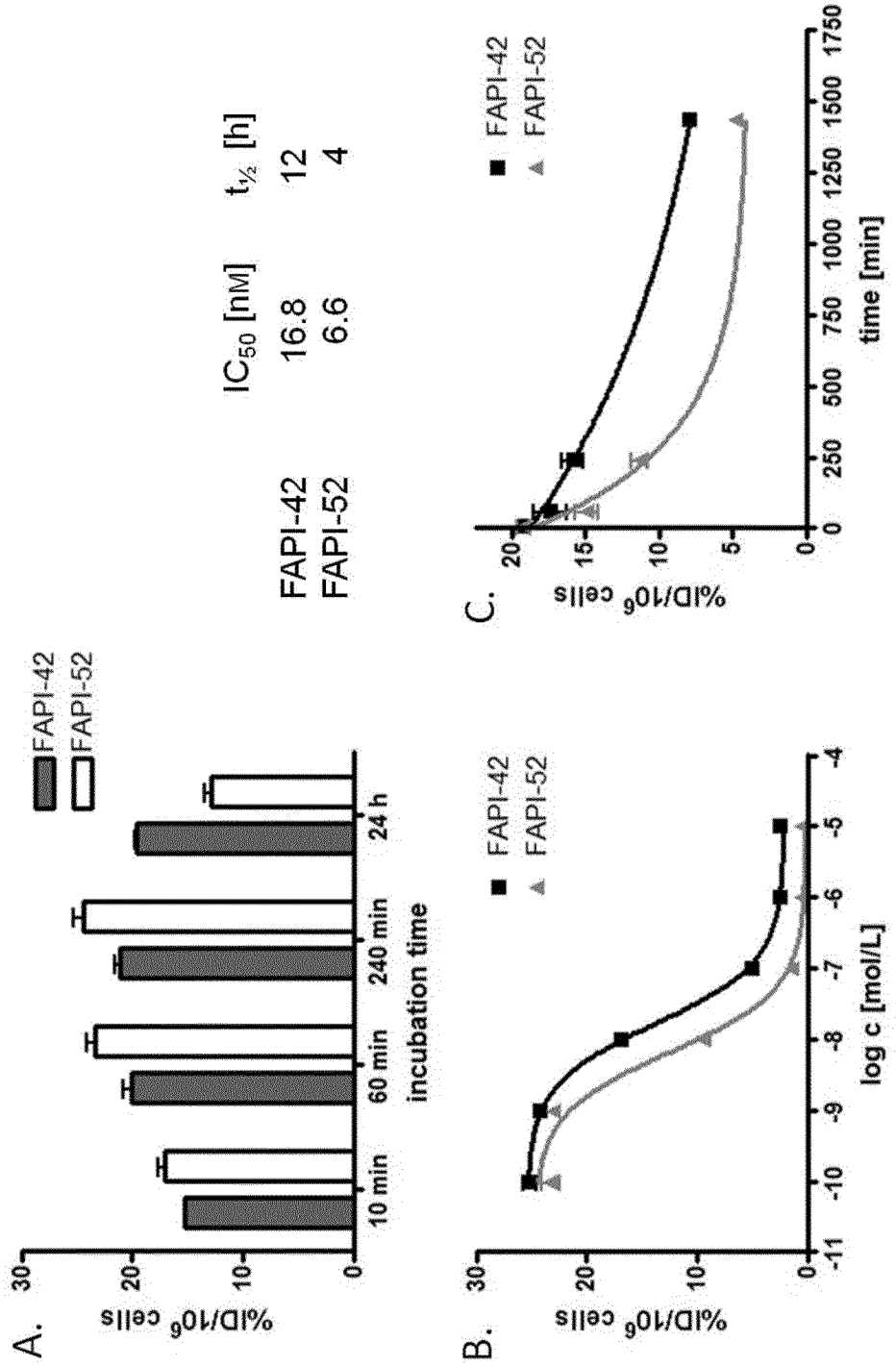

A.
FAPI-42
FAPI-52
%ID/10^6 cells
incubation time
10 min
60 min
240 min
24 h
B.
log c [mol/L]
C.
time [min]
IC50 [nM]
t½ [h]
FAPI-42 16.8 12
FAPI-52 6.6 4

Figure 38

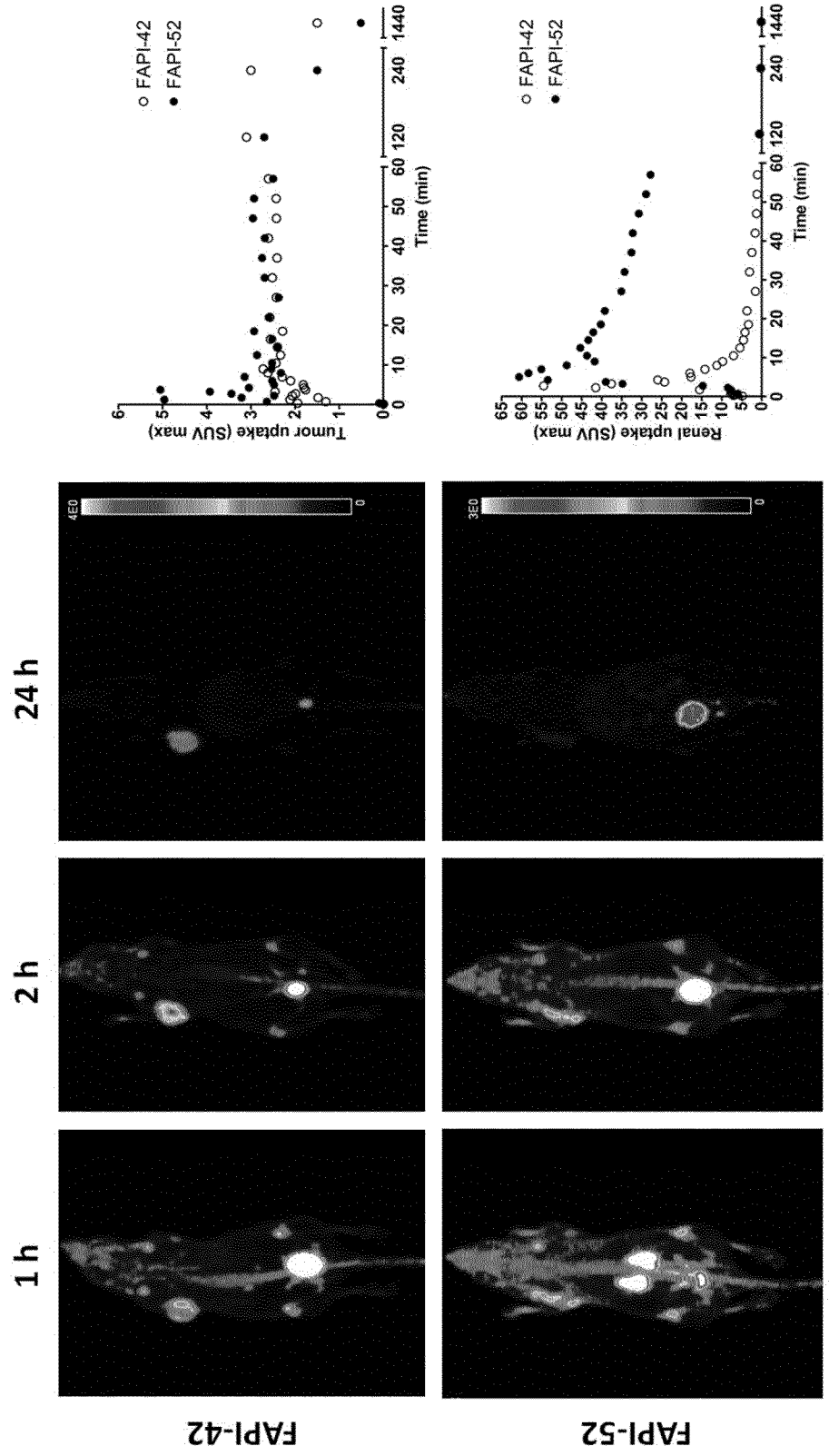

FAPI-42
FAPI-52
1 h
2 h
24 h
Renal uptake (SUV max)
Tumor uptake (SUV max)
Time (min)
0
10
20
30
40
50
60
120
240
1440

Figure 39

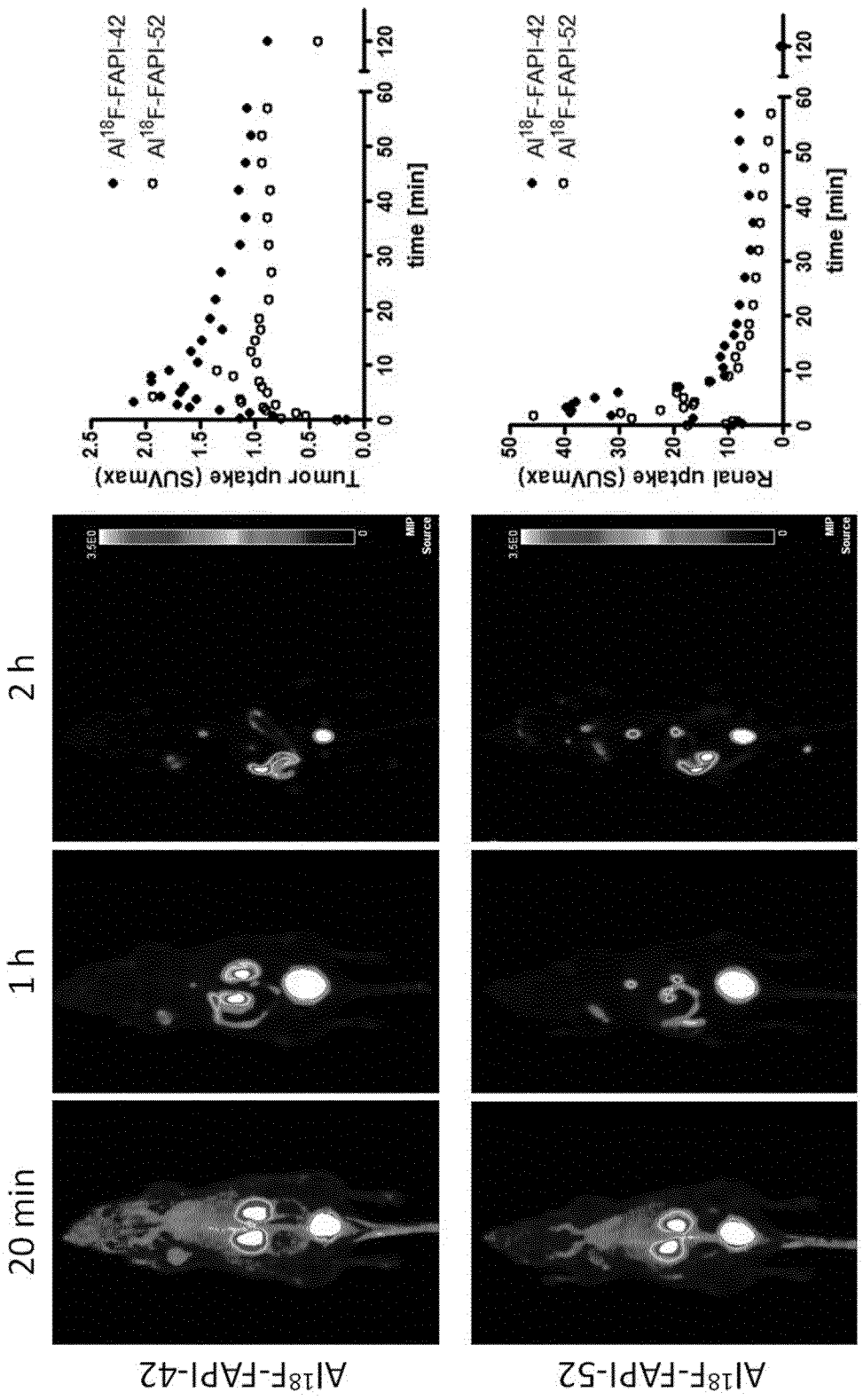

20 min
1 h
2 h
Al18F-FAPI-42
Al18F-FAPI-52
Tumor uptake (SUVmax)
Renal uptake (SUVmax)
time [min]
Al18F-FAPI-42
Al18F-FAPI-52

Figure 40

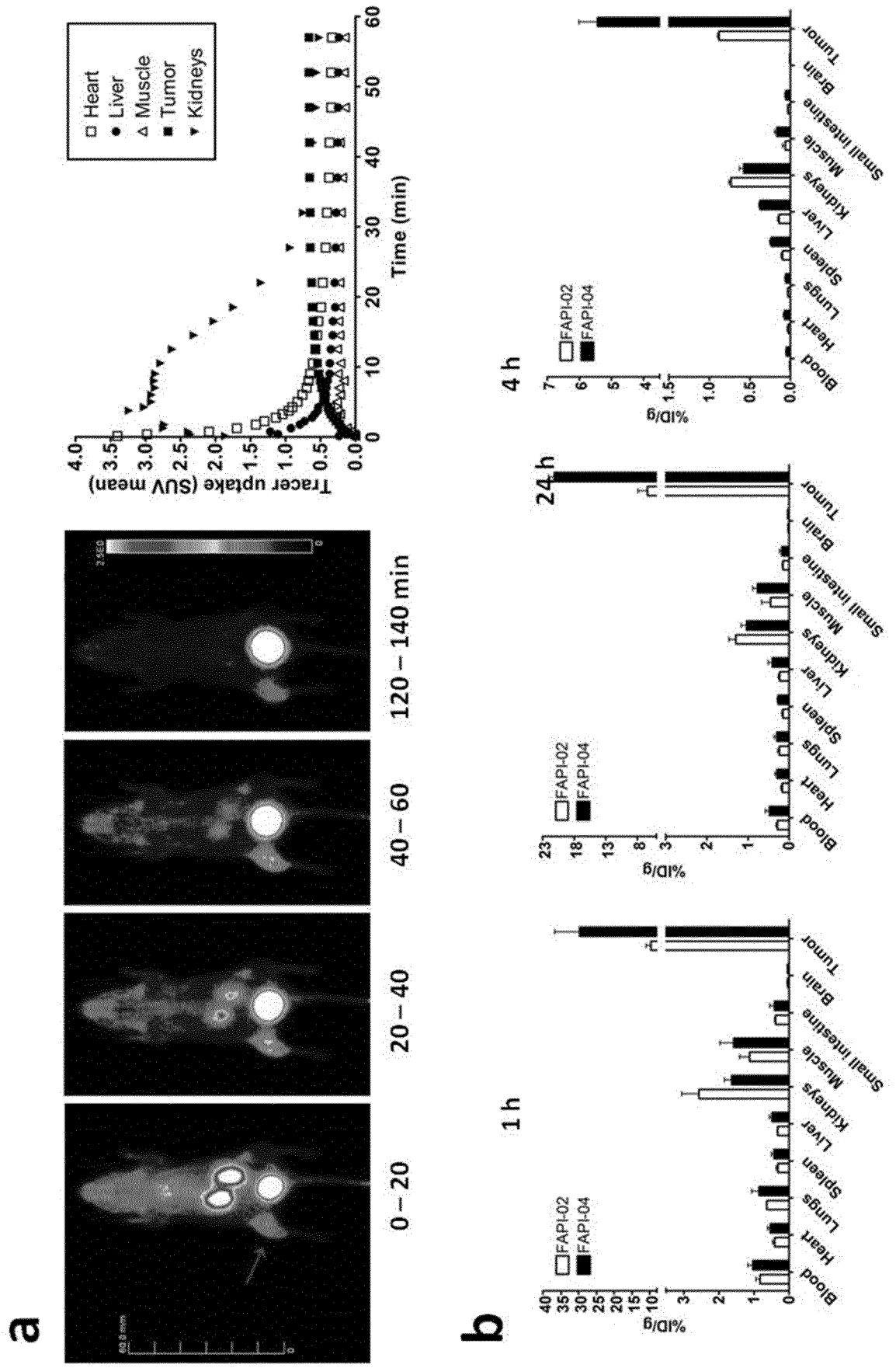

a
0 – 20
20 – 40
40 – 60
120 – 140 min
Tracer uptake (SUV mean)
Time (min)
Heart
Liver
Muscle
Tumor
Kidneys
b
1 h
4 h
24 h
%ID/g
FAPI-02
FAPI-04
Blood
Heart
Lungs
Spleen
Liver
Kidneys
Muscle
Small intestine
Brain
Tumor

Figure 41

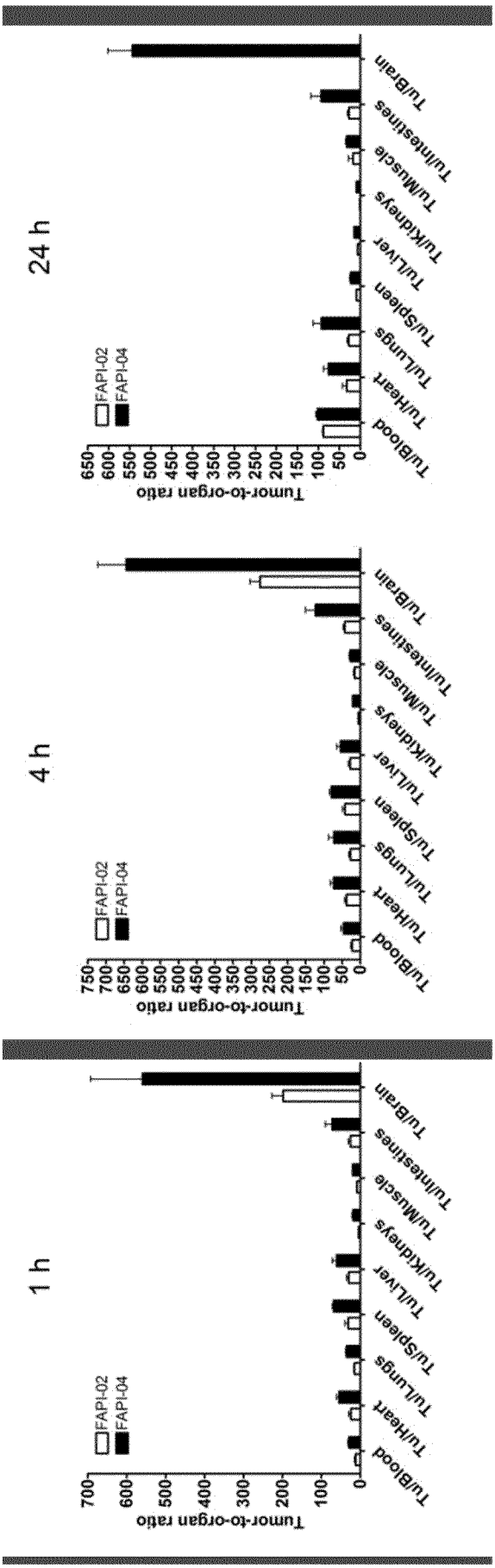

24 h
4 h
1 h
FAPI-02
FAPI-04
Tumor-to-organ ratio
Tu/Blood
Tu/Heart
Tu/Lungs
Tu/Spleen
Tu/Liver
Tu/Kidneys
Tu/Muscle
Tu/Intestines
Tu/Brain

Figure 42

Figure 43

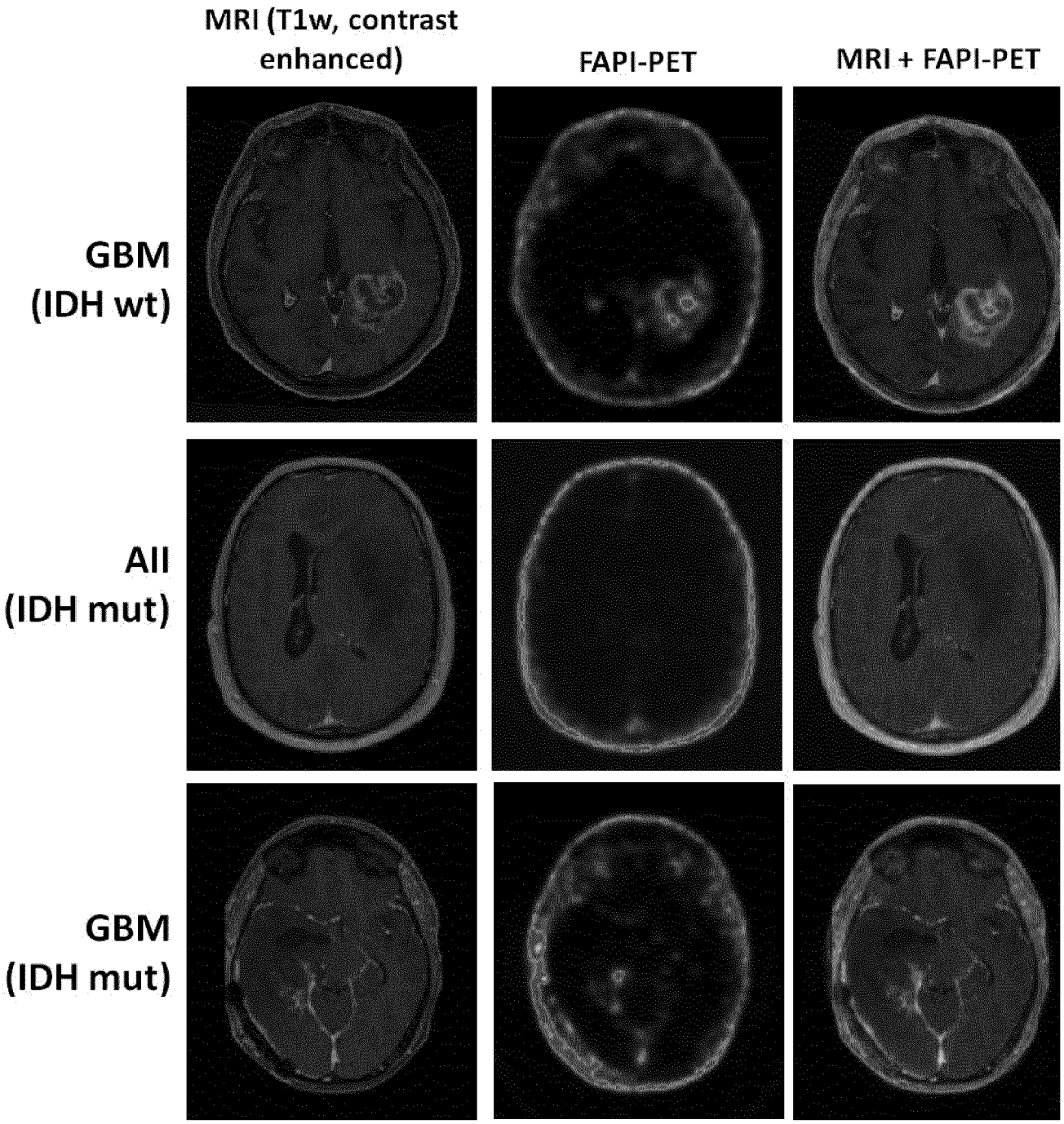

MRI (T1w, contrast enhanced)
FAPI-PET
MRI + FAPI-PET
GBM (IDH wt)
AII (IDH mut)
GBM (IDH mut)

Figure 44

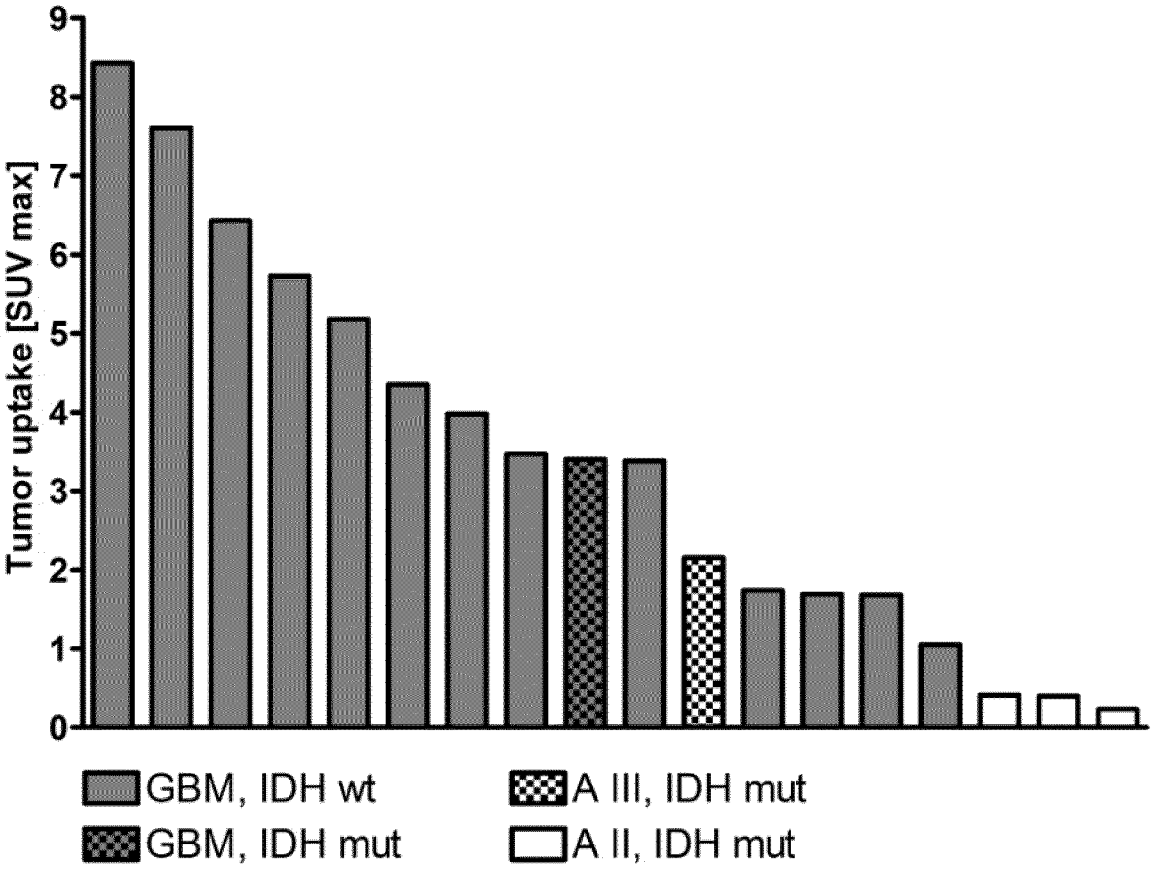

Tumor uptake [SUV max]
9
8
7
6
5
4
3
2
1
0
GBM, IDH wt
GBM, IDH mut
A III, IDH mut
A II, IDH mut

Figure 45

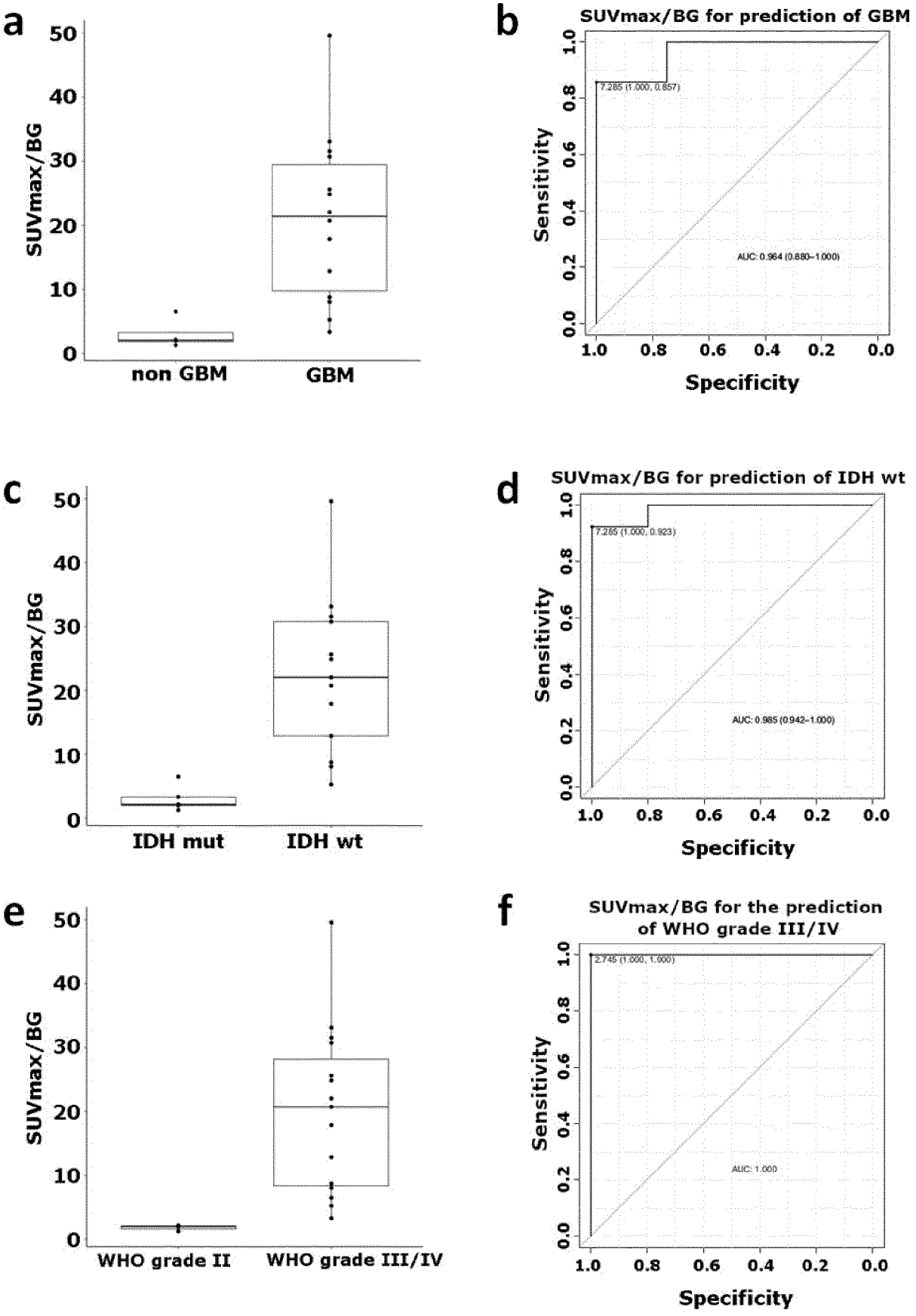

a
SUVmax/BG
50
40
30
20
10
0
non GBM
GBM
b
SUVmax/BG for prediction of GBM
7.285 (1.000, 0.857)
AUC: 0.964 (0.880–1.000)
Sensitivity
Specificity
1.0
0.8
0.6
0.4
0.2
0.0
c
SUVmax/BG
IDH mut
IDH wt
d
SUVmax/BG for prediction of IDH wt
7.285 (1.000, 0.923)
AUC: 0.985 (0.942–1.000)
e
SUVmax/BG
WHO grade II
WHO grade III/IV
f
SUVmax/BG for the prediction of WHO grade III/IV
2.745 (1.000, 1.000)
AUC: 1.000

Figure 46

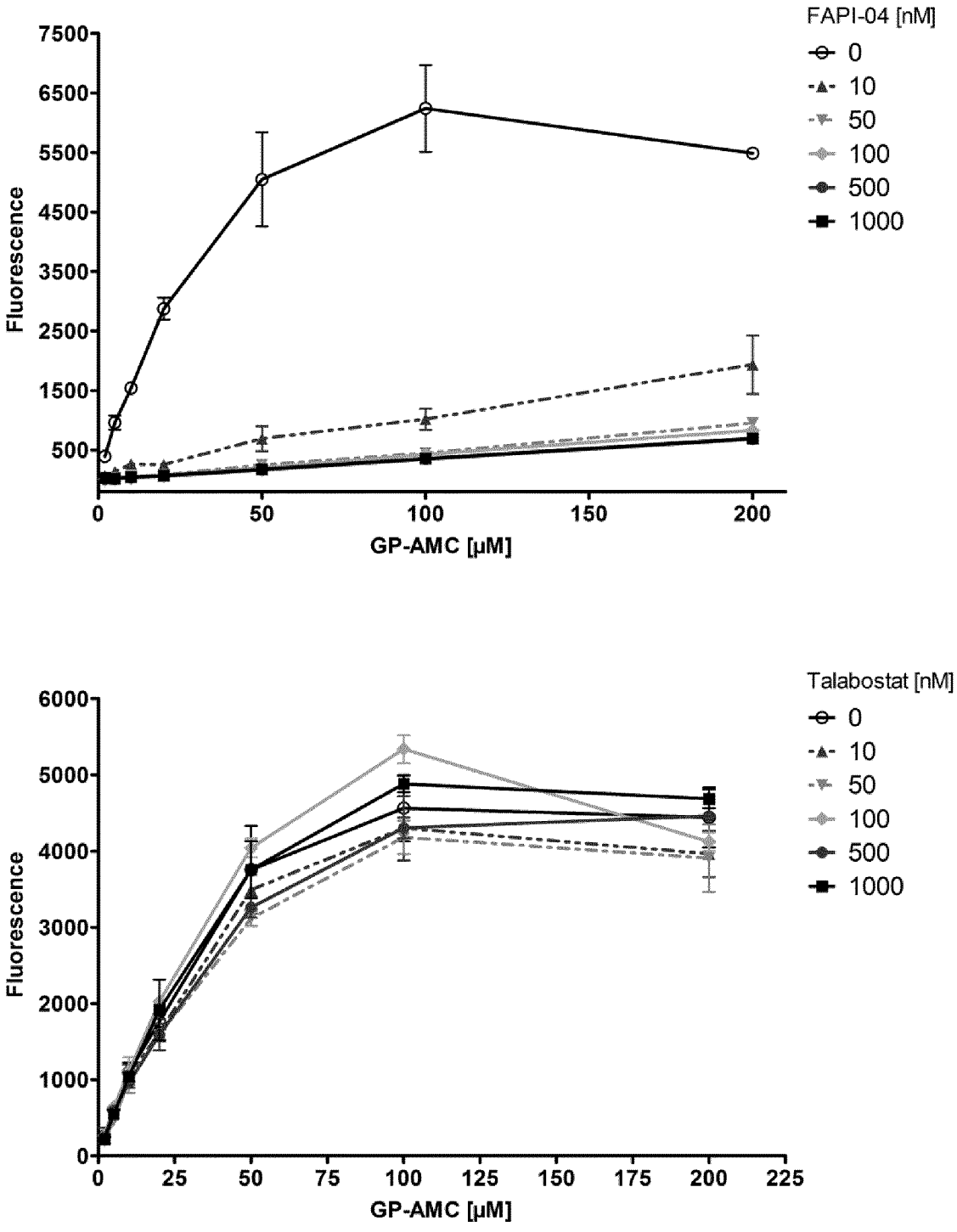

FAPI-04 [nM]
0
10
50
100
500
1000
Fluorescence
7500
6500
5500
4500
3500
2500
1500
500
0
50
100
150
200
GP-AMC [µM]
Talabostat [nM]
0
10
50
100
500
1000
Fluorescence
6000
5000
4000
3000
2000
1000
0
0
25
50
75
100
125
150
175
200
225
GP-AMC [µM]

Figure 47

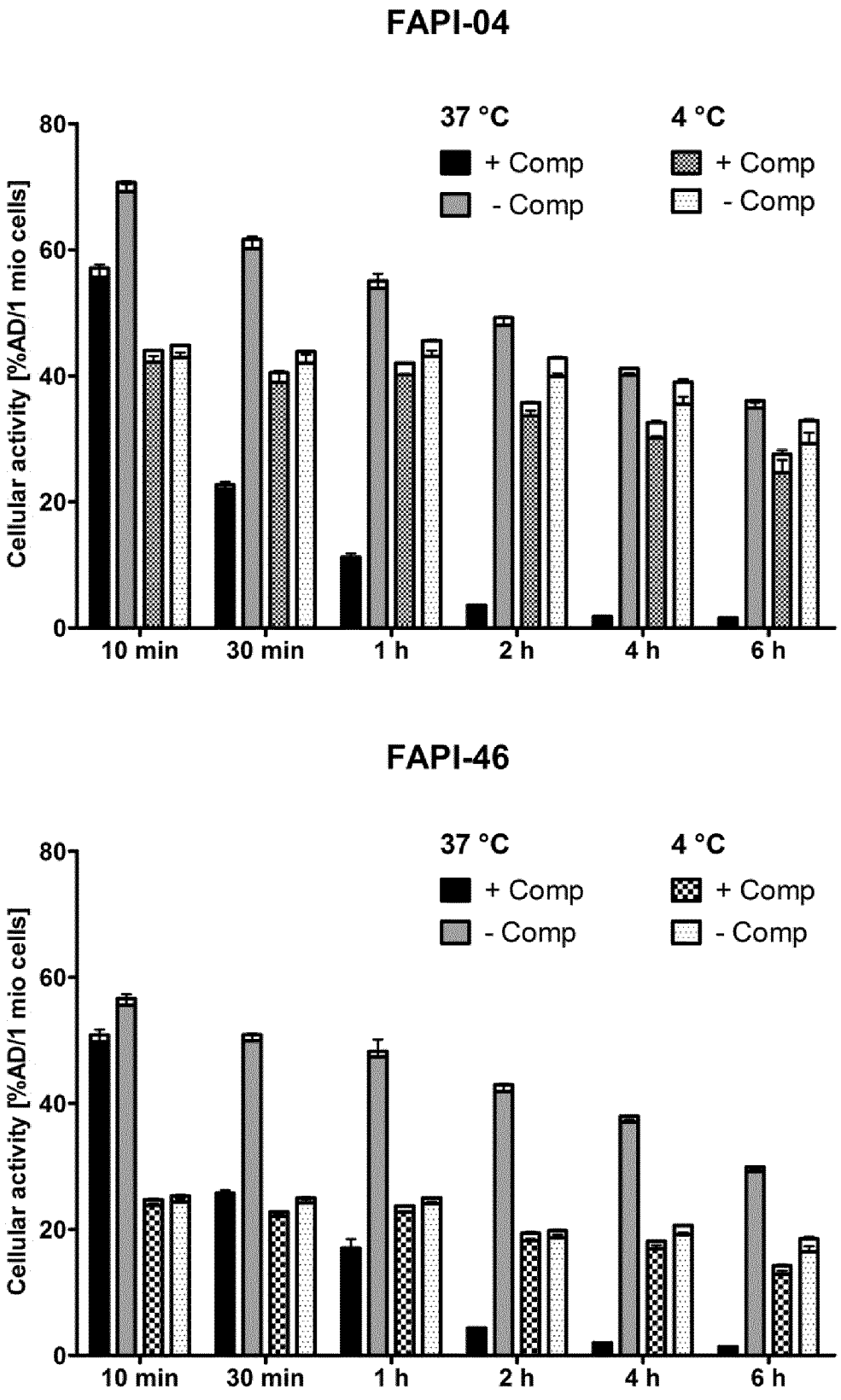

FAPI-04
37 °C
+ Comp
- Comp
4 °C
+ Comp
- Comp
Cellular activity [%AD/1 mio cells]
0
20
40
60
80
10 min
30 min
1 h
2 h
4 h
6 h
FAPI-46
37 °C
+ Comp
- Comp
4 °C
+ Comp
- Comp
Cellular activity [%AD/1 mio cells]
0
20
40
60
80
10 min
30 min
1 h
2 h
4 h
6 h

Figure 48

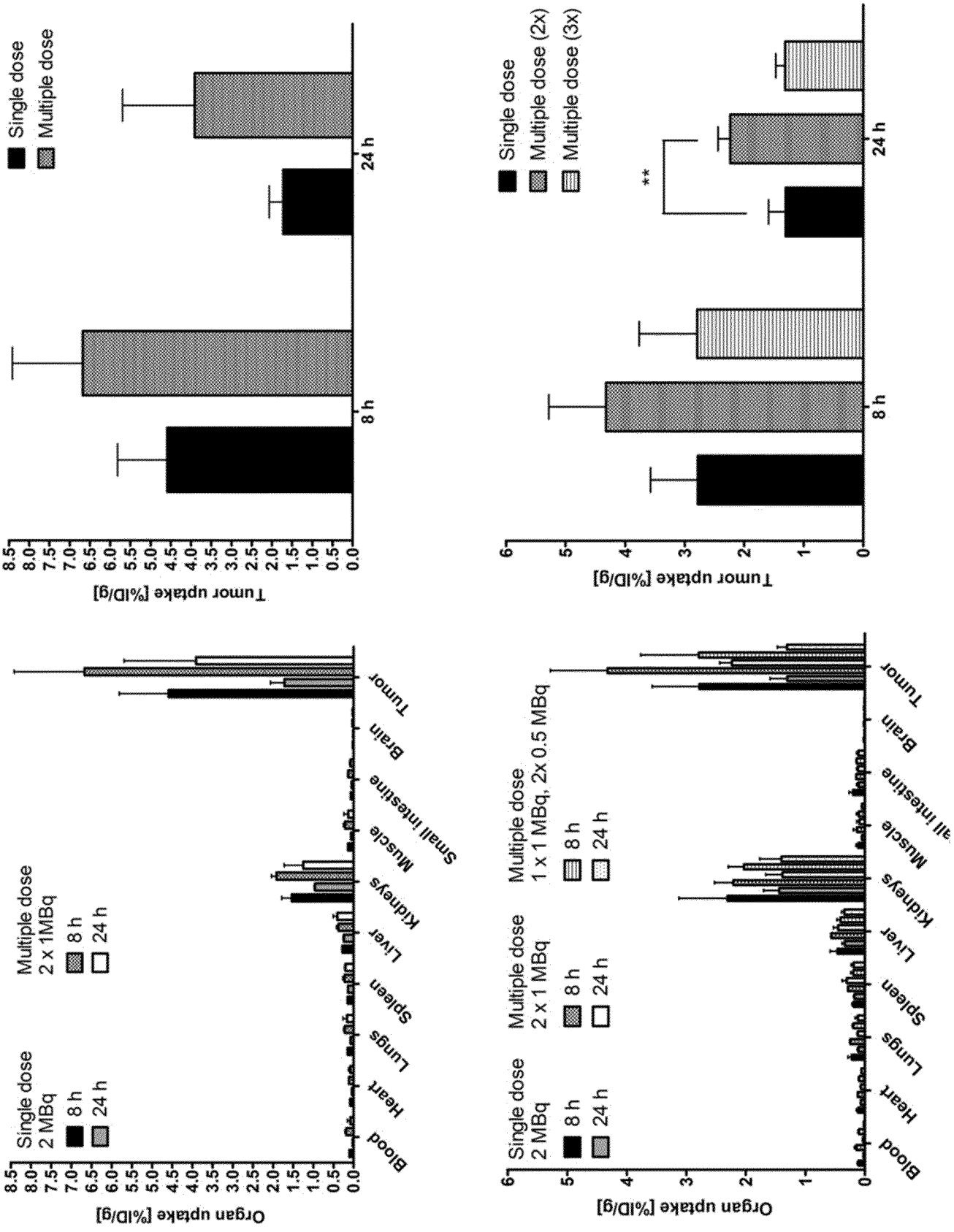

Single dose
Multiple dose
Tumor uptake [%ID/g]
8 h
24 h
Single dose
Multiple dose (2x)
Multiple dose (3x)
**
Organ uptake [%ID/g]
Single dose
2 MBq
8 h
24 h
Multiple dose
2 x 1MBq
Multiple dose
2 x 1 MBq
Multiple dose
1 x 1 MBq, 2x 0.5 MBq
Blood
Heart
Lungs
Spleen
Liver
Kidneys
Muscle
Small intestine
Brain
Tumor

Figure 49

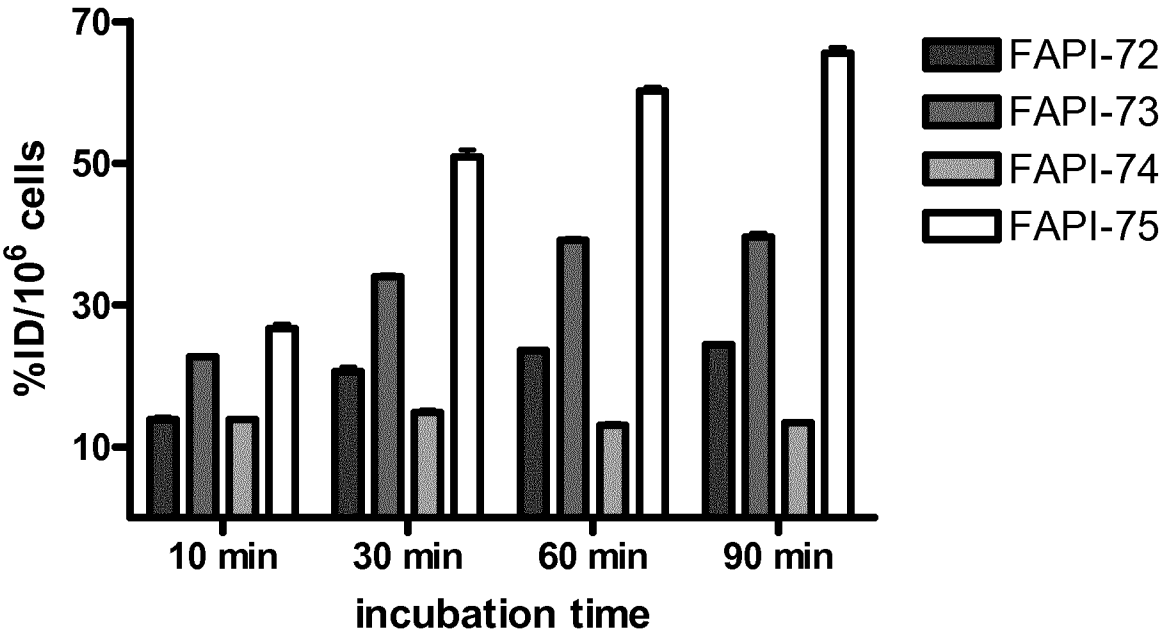

70
50
30
10
%ID/10^6 cells
10 min
30 min
60 min
90 min
incubation time
FAPI-72
FAPI-73
FAPI-74
FAPI-75

Figure 50

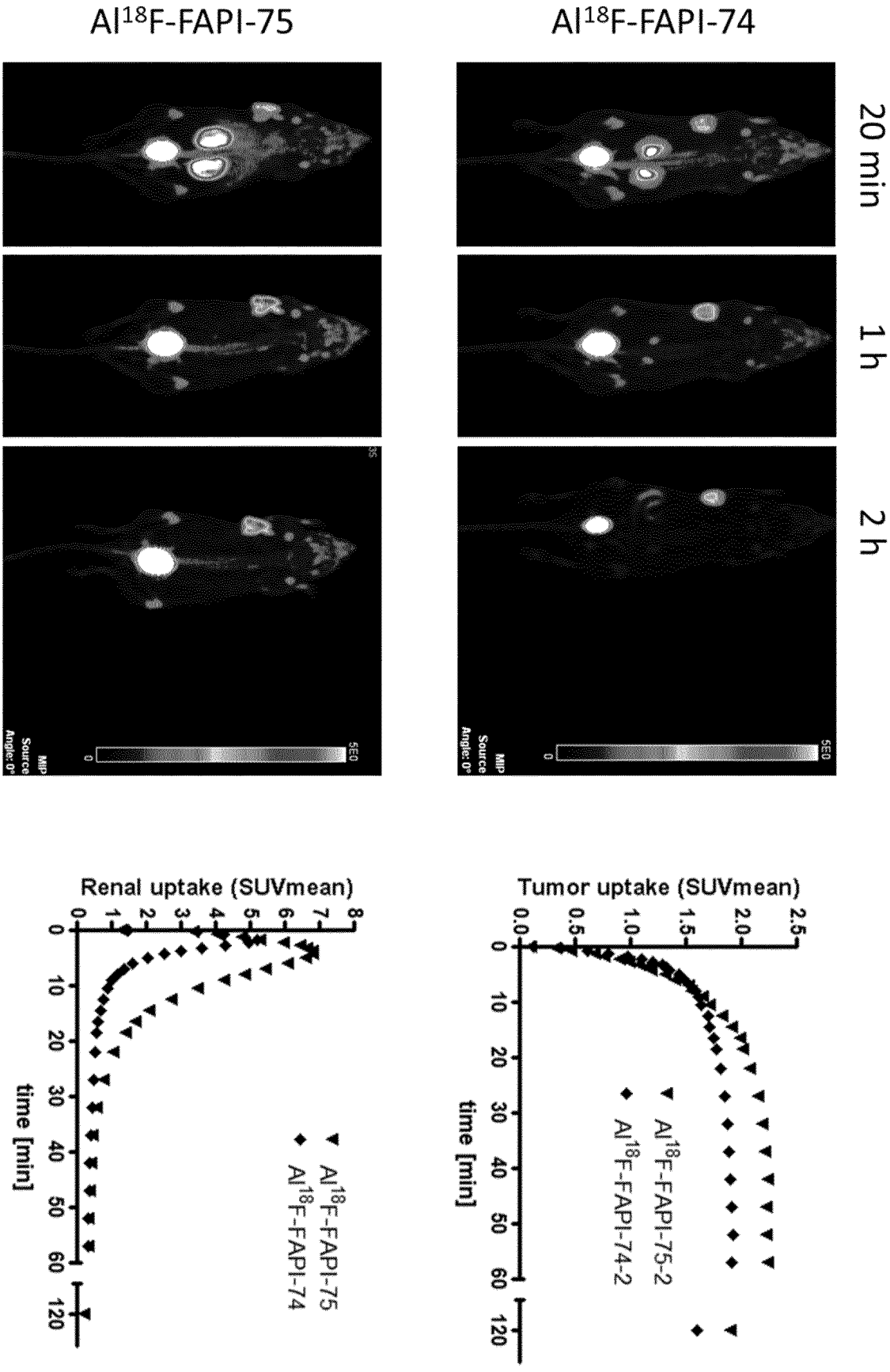

Al18F-FAPI-75
Al18F-FAPI-74
20 min
1 h
2 h
Renal uptake (SUVmean)
time [min]
Al18F-FAPI-75
Al18F-FAPI-74
Tumor uptake (SUVmean)
time [min]
Al18F-FAPI-75-2
Al18F-FAPI-74-2

Figure 51

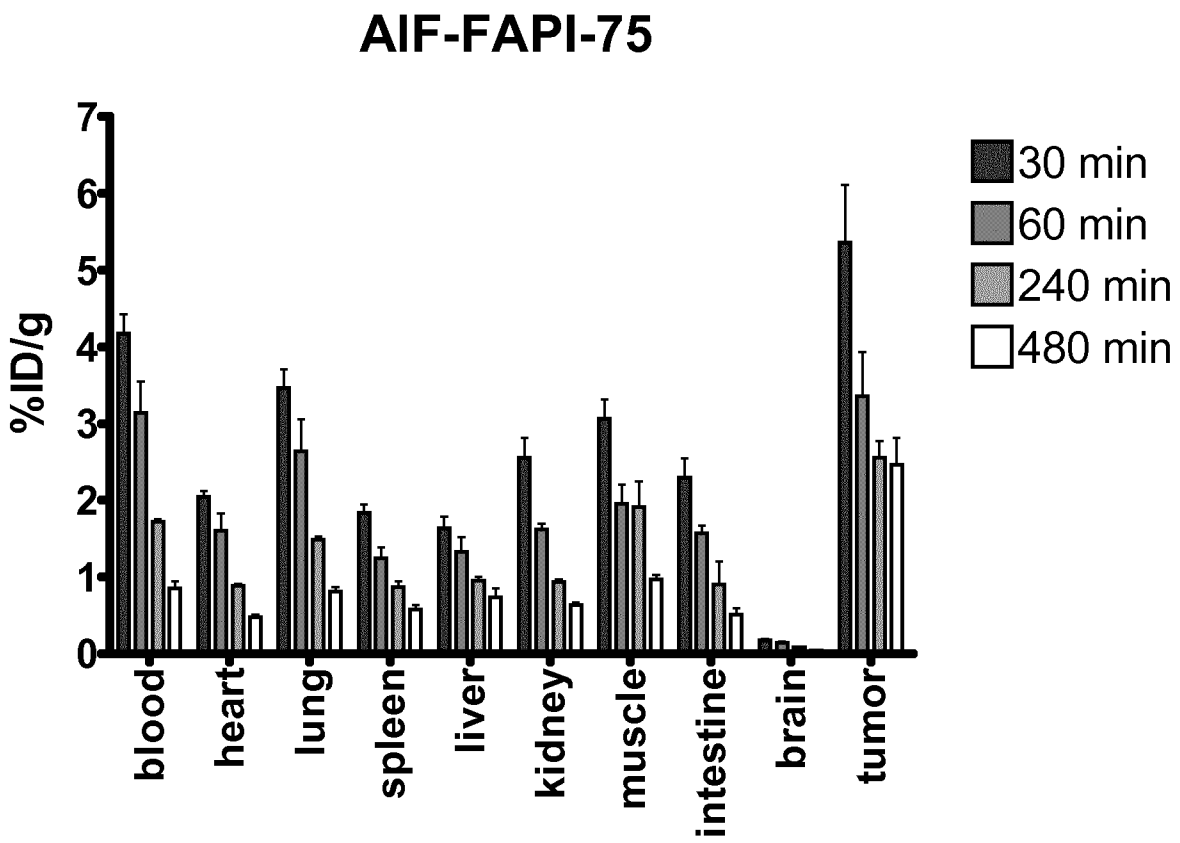

AlF-FAPI-75
%ID/g
0
1
2
3
4
5
6
7
blood
heart
lung
spleen
liver
kidney
muscle
intestine
brain
tumor
30 min
60 min
240 min
480 min

Figure 52

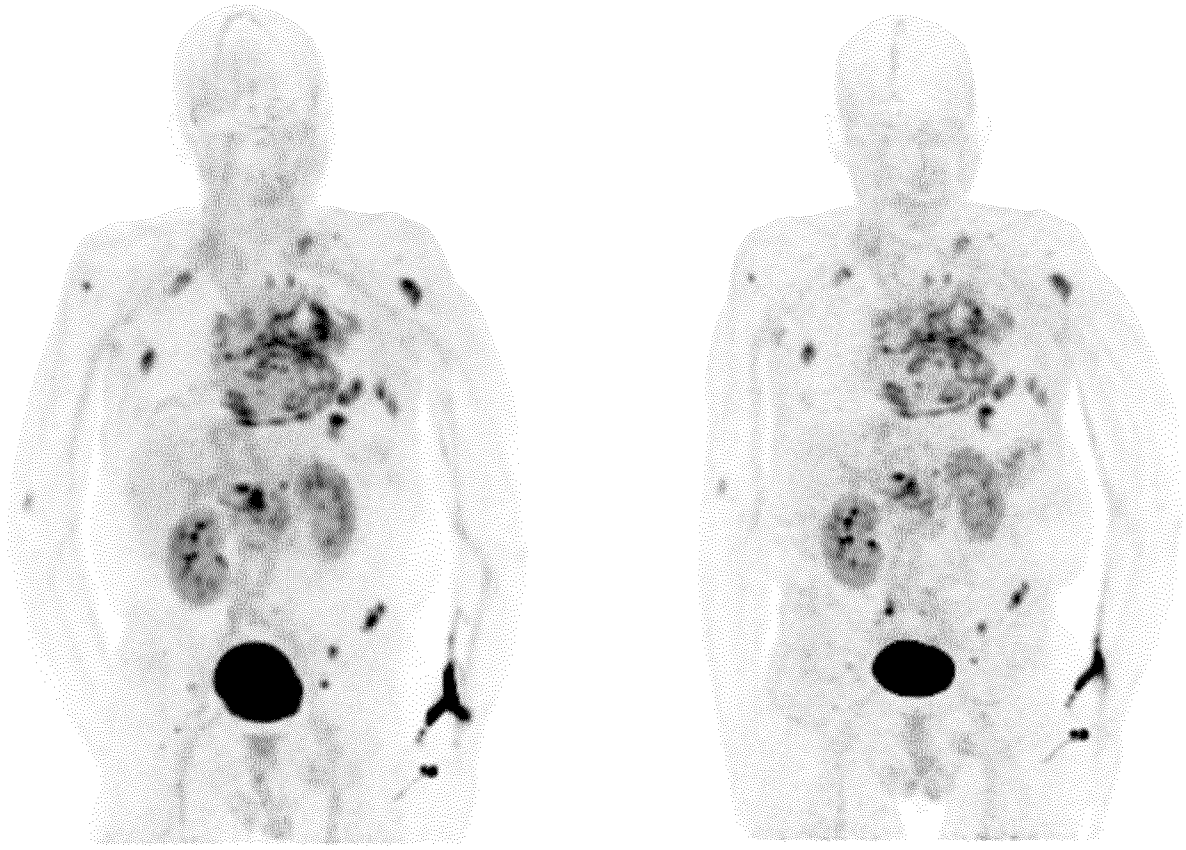


Figure 53

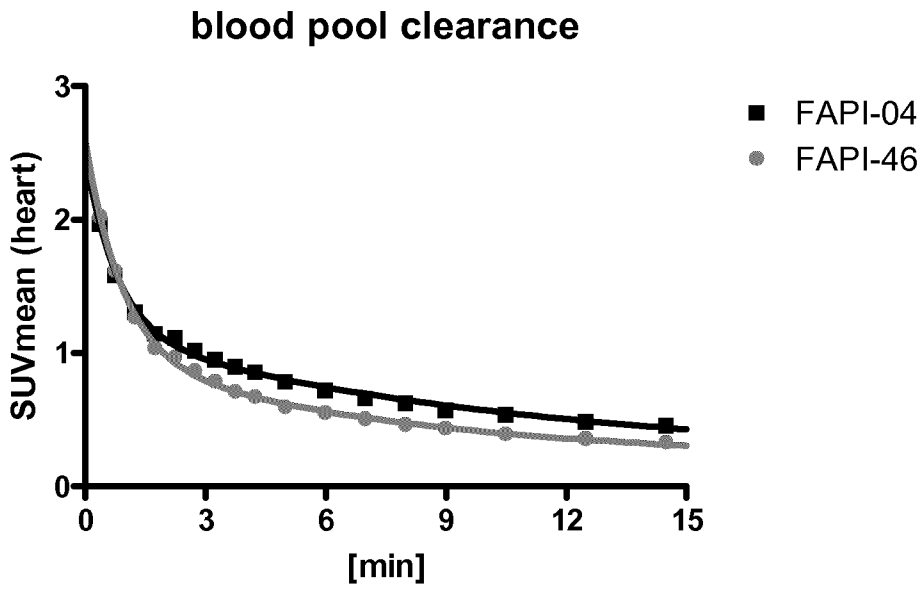


Figure 54

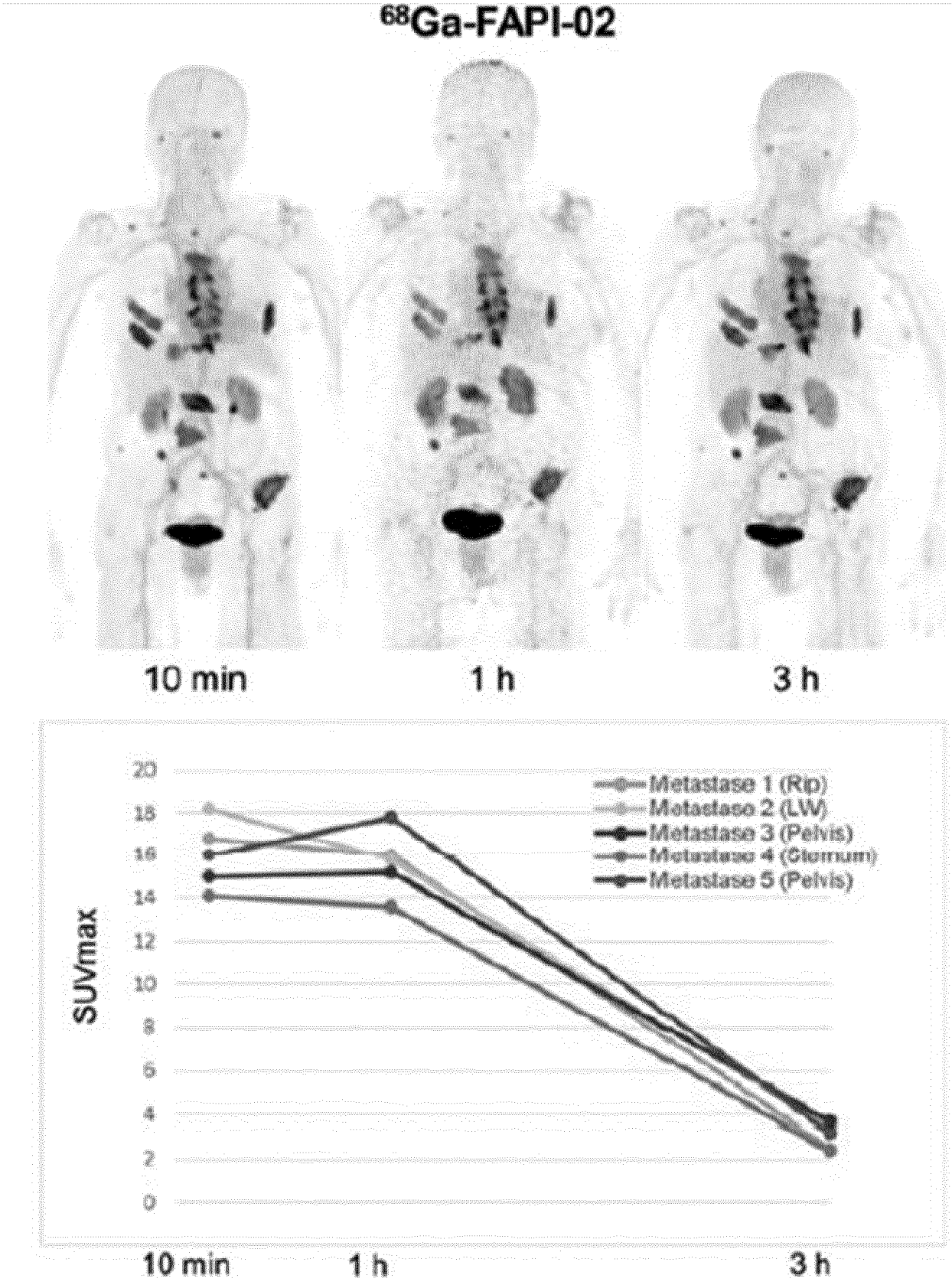

68Ga-FAPI-02
10 min
1 h
3 h
SUVmax
20
18
16
14
12
10
8
6
4
2
0
Metastase 1 (Rip)
Metastase 2 (LW)
Metastase 3 (Pelvis)
Metastase 4 (Clomum)
Metastase 5 (Pelvis)
10 min
1 h
3 h

Figure 54 continued

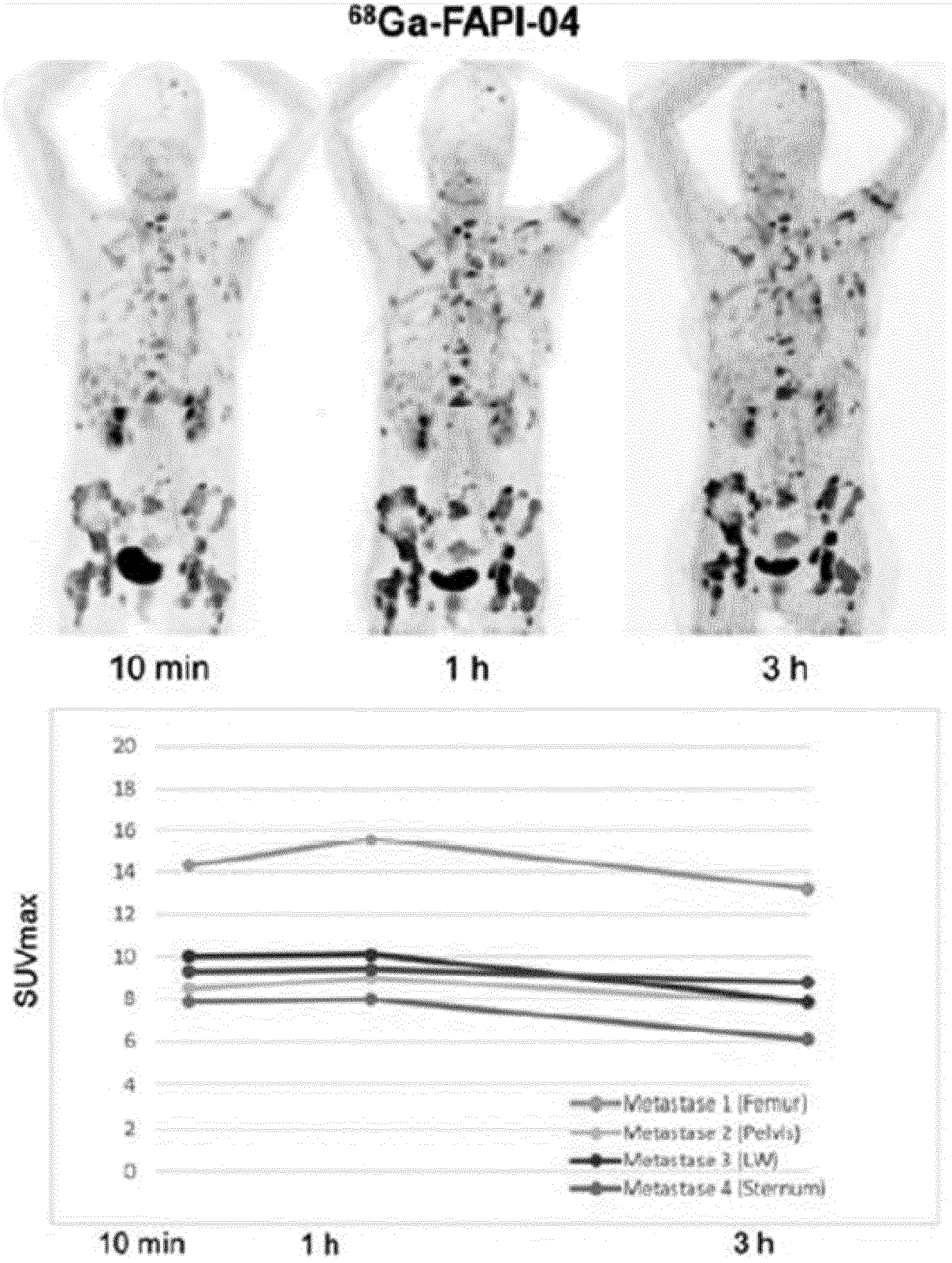


Figure 55

	FAPI-2	FAPI-4
Adrenals	1.23E-02	1.12E-02
Brain	9.54E-03	9.11E-03
Breasts	9.58E-03	8.88E-03
Gallbladder Wall	1.19E-02	1.13E-02
LLI Wall	1.23E-02	1.17E-02
Small Intestine	1.19E-02	1.13E-02
Stomach Wall	1.13E-02	1.06E-02
ULI Wall	1.17E-02	1.11E-02
Heart Wall	4.73E-02	2.02E-02
Kidneys	4.45E-02	4.43E-02
Liver	1.51E-02	1.46E-02
Lungs	1.09E-02	9.89E-03
Muscle	1.04E-02	9.91E-03
Ovaries	1.24E-02	1.19E-02
Pancreas	1.23E-02	1.13E-02
Red Marrow	3.28E-02	2.08E-02
Osteogenic Cells	2.94E-02	2.16E-02
Skin	9.01E-03	8.63E-03
Spleen	2.62E-02	1.05E-02
Testes	1.04E-02	1.01E-02
Thymus	1.15E-02	1.01E-02
Thyroid	1.03E-02	9.82E-03
Urinary Bladder Wall	8.89E-02	9.91E-02
Uterus	1.33E-02	1.30E-02
Total Body	1.19E-02	1.09E-02
Effective Dose (mSv/MBq)	1.80E-02	1.64E-02

Figure 56

A)

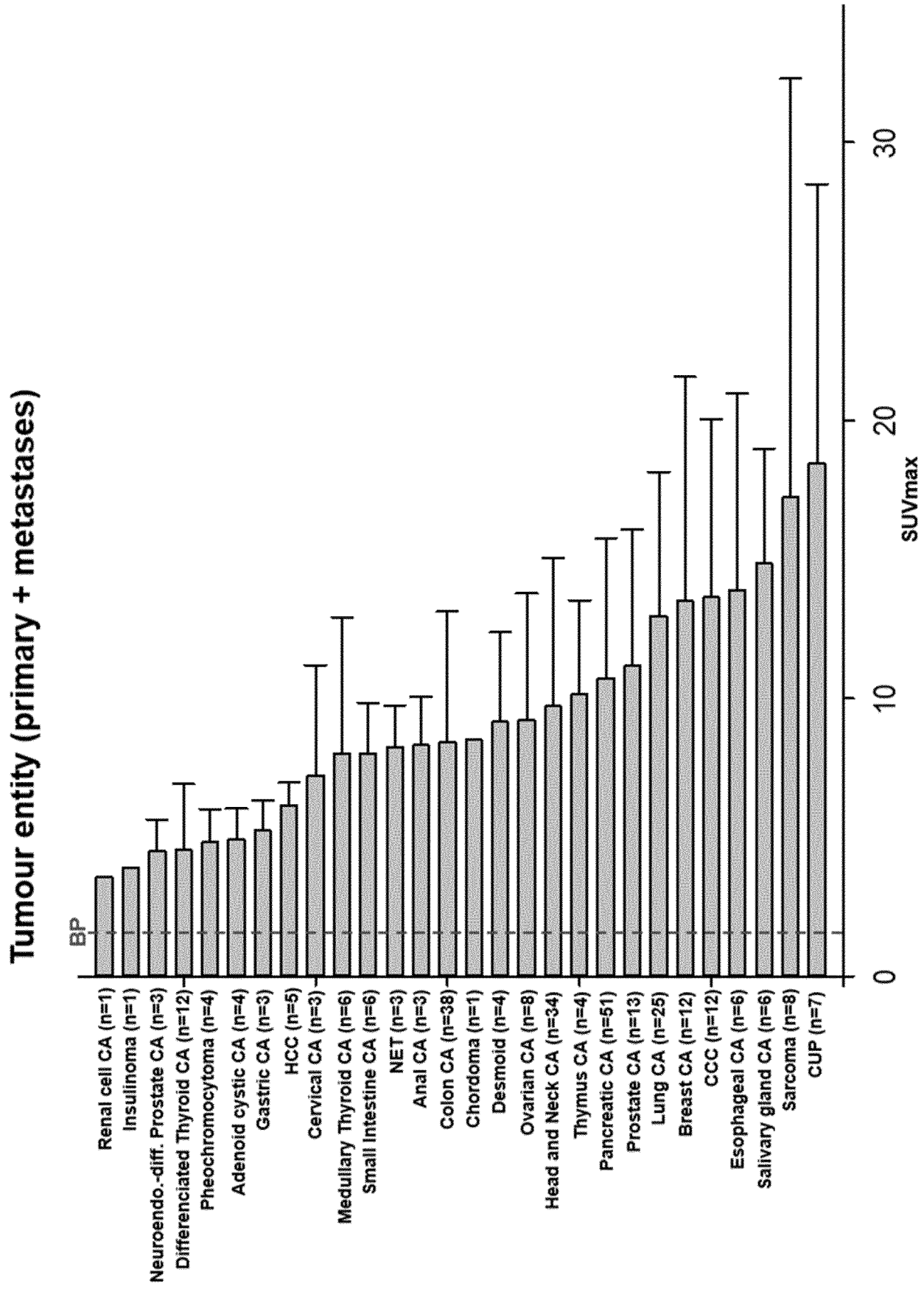

Tumour entity (primary + metastases)
BP
Renal cell CA (n=1)
Insulinoma (n=1)
Neuroendo.-diff. Prostate CA (n=3)
Differenciated Thyroid CA (n=12)
Pheochromocytoma (n=4)
Adenoid cystic CA (n=4)
Gastric CA (n=3)
HCC (n=5)
Cervical CA (n=3)
Medullary Thyroid CA (n=6)
Small Intestine CA (n=6)
NET (n=3)
Anal CA (n=3)
Colon CA (n=38)
Chordoma (n=1)
Desmoid (n=4)
Ovarian CA (n=8)
Head and Neck CA (n=34)
Thymus CA (n=4)
Pancreatic CA (n=51)
Prostate CA (n=13)
Lung CA (n=25)
Breast CA (n=12)
CCC (n=12)
Esophageal CA (n=6)
Salivary gland CA (n=6)
Sarcoma (n=8)
CUP (n=7)
0
10
20
30
SUVmax

Figure 56 continued

B)

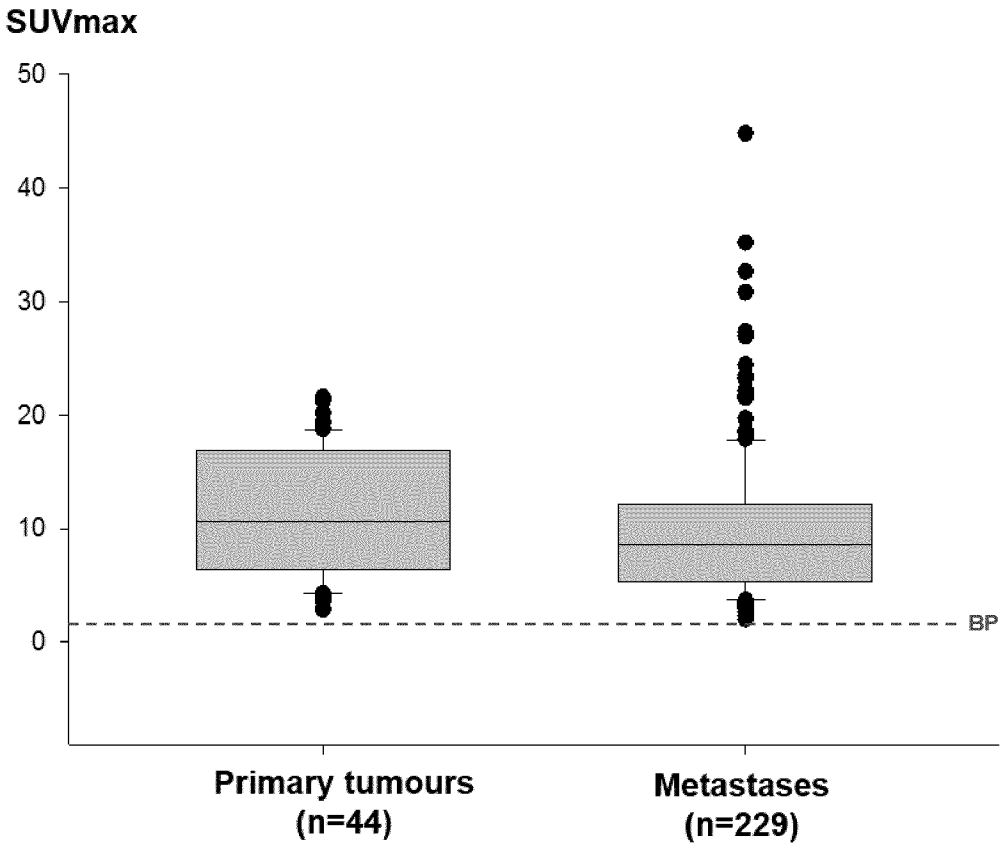


Figure 57

