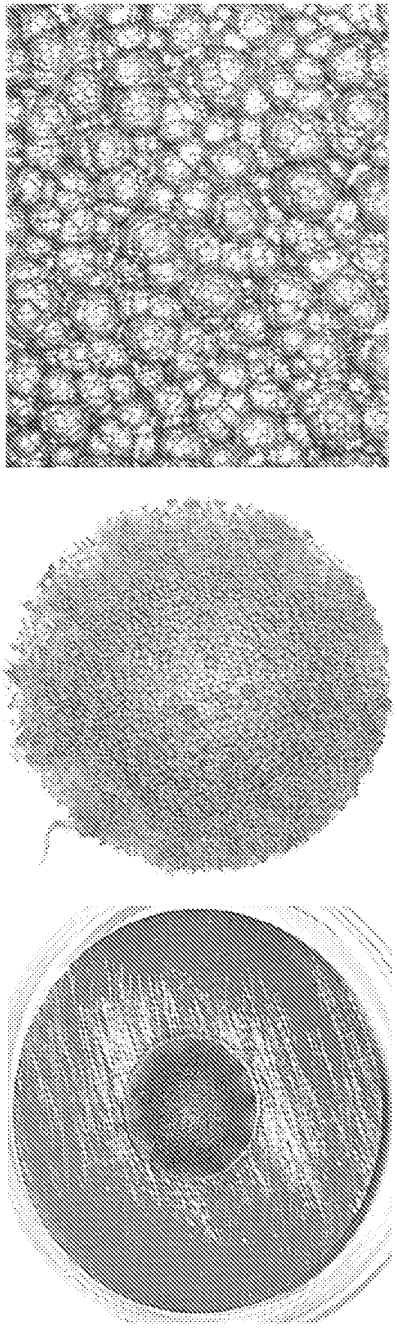


FIG. 1

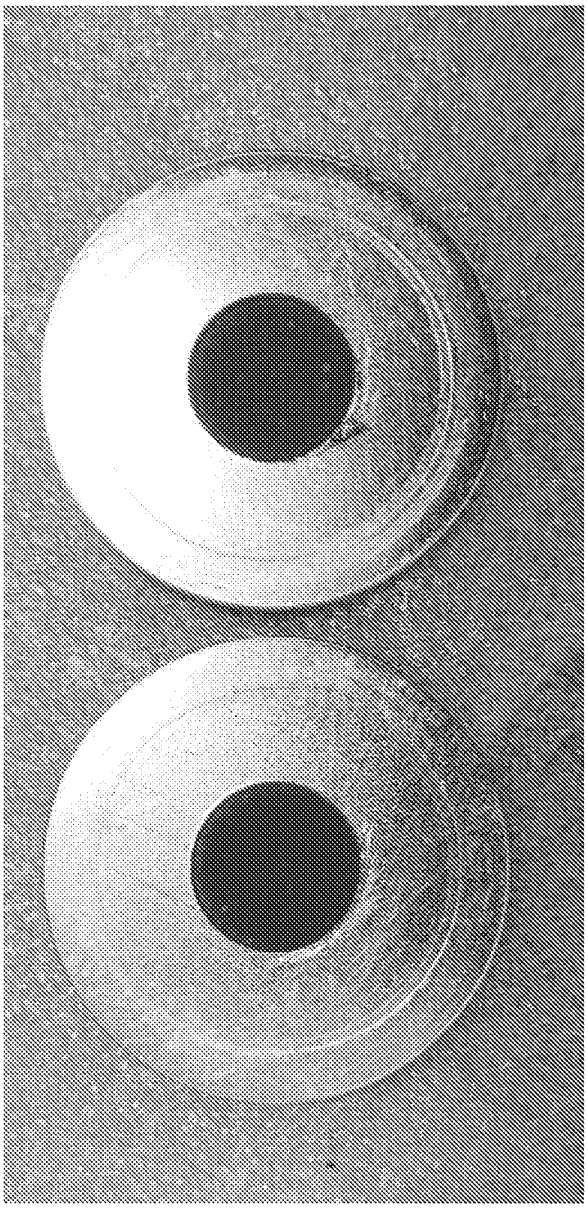


FIG. 2

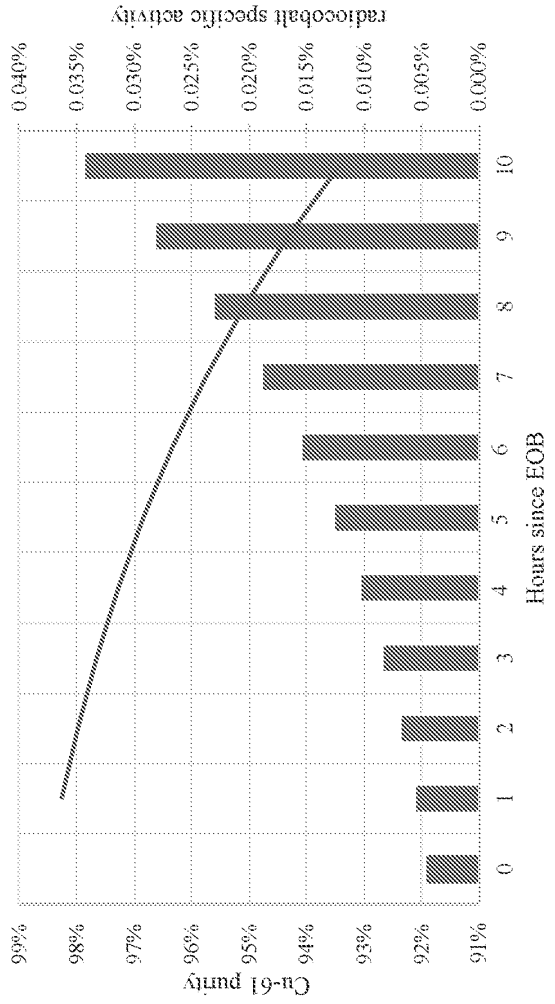

radiocobalt specific activity
0.040%
0.035%
0.030%
0.025%
0.020%
0.015%
0.010%
0.005%
0.000%
Cu-61 purity
99%
98%
97%
96%
95%
94%
93%
92%
91%
0
1
2
3
4
5
6
7
8
9
10
Hours since EOB

FIG. 3

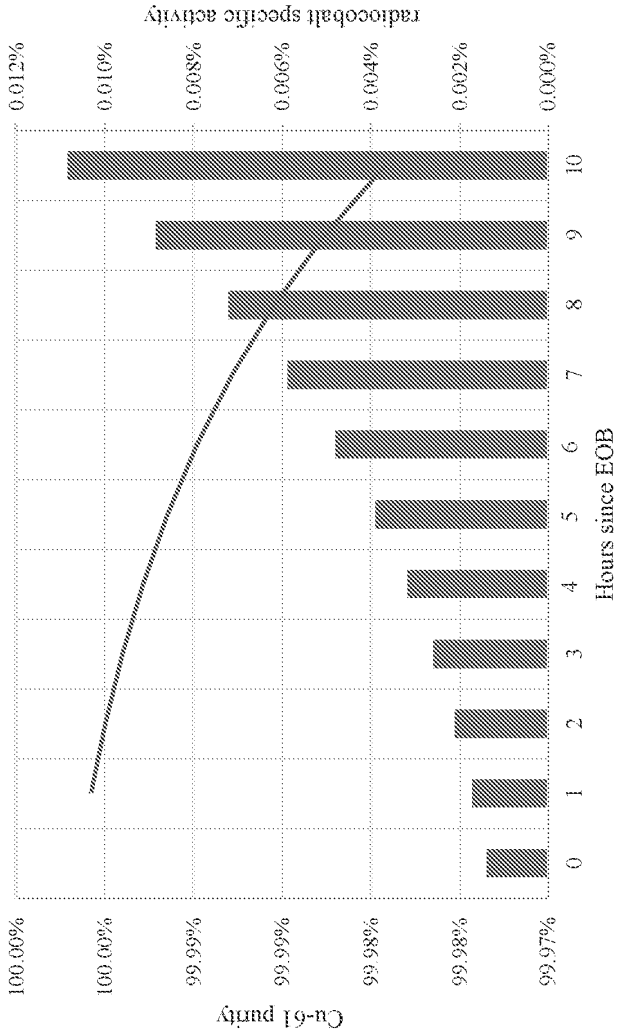

radiocobalt specific activity
0.012%
0.010%
0.008%
0.006%
0.004%
0.002%
0.000%
Cu-61 purity
100.00%
100.00%
99.99%
99.99%
99.98%
99.98%
99.97%
0
1
2
3
4
5
6
7
8
9
10
Hours since EOB

FIG. 4

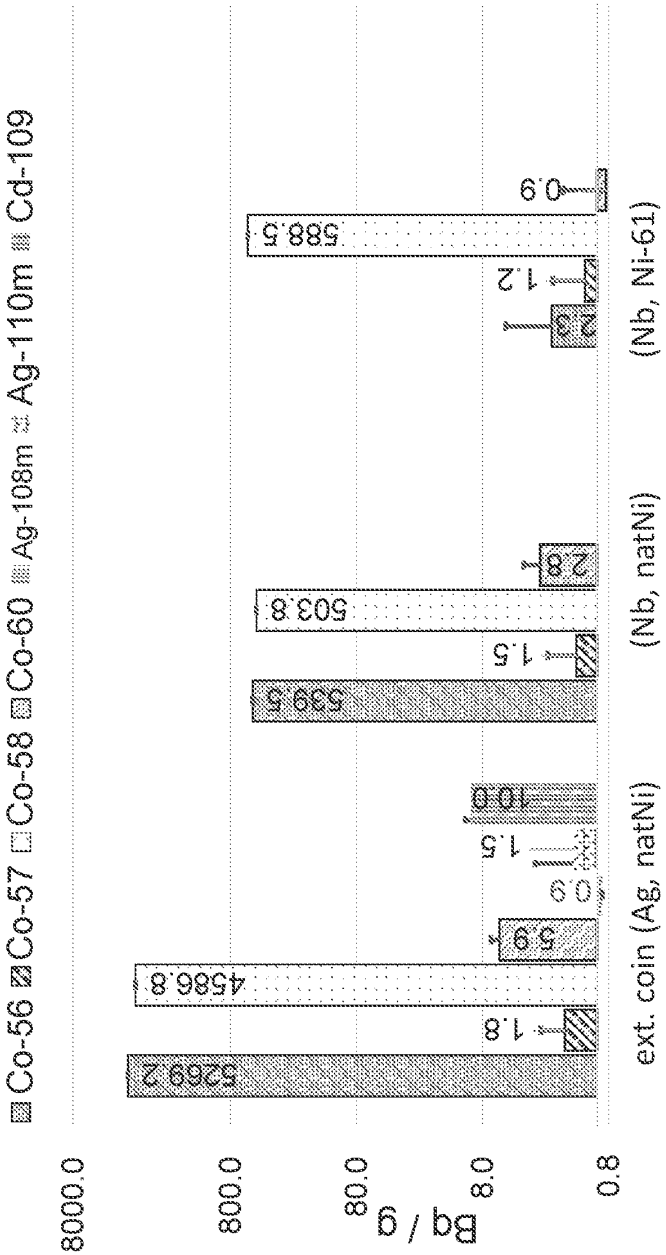

Specific activity of detected impurities in the Cu-61 product
Co-56 Co-57 Co-58 Co-60 Ag-108m Ag-110m Cd-109
8000.0
800.0
80.0
8.0
0.8
Bq / g
5269.2
1.8
4586.8
5.9
0.9
1.5
10.0
539.5
1.5
503.8
2.8
588.5
0.9
1.2
2.3
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 5

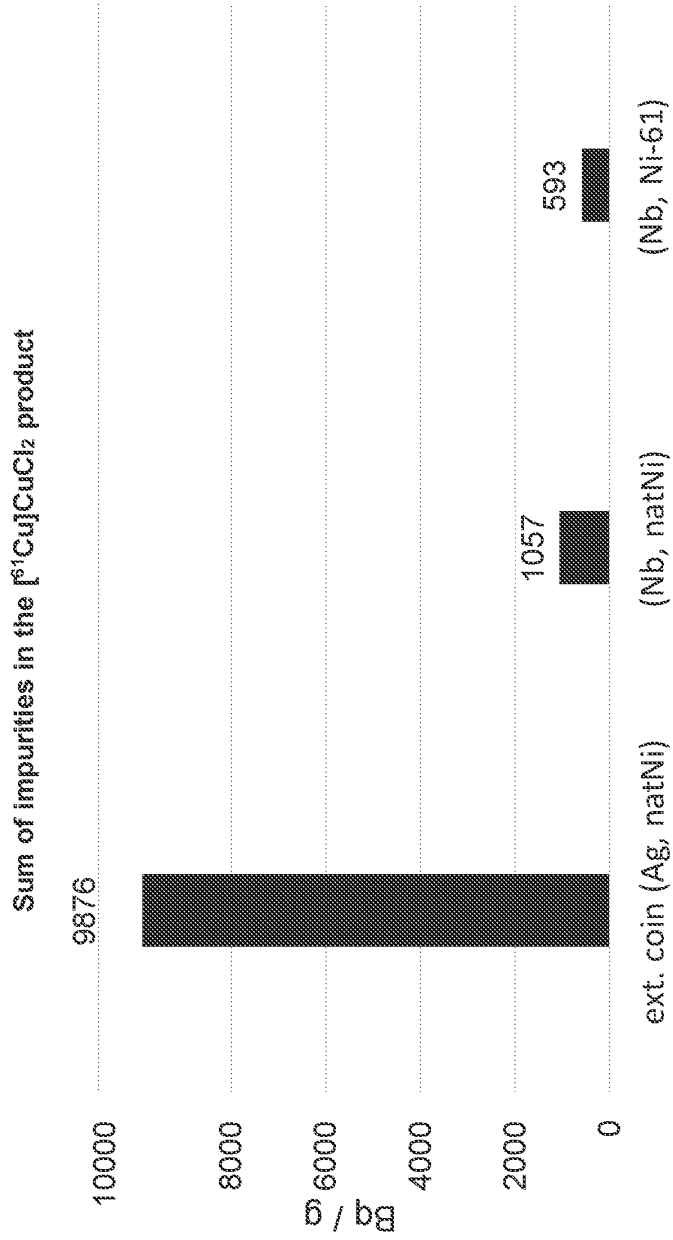

Sum of impurities in the [61Cu]CuCl2 product
Bq / g
10000
8000
6000
4000
2000
0
9876
1057
593
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 6

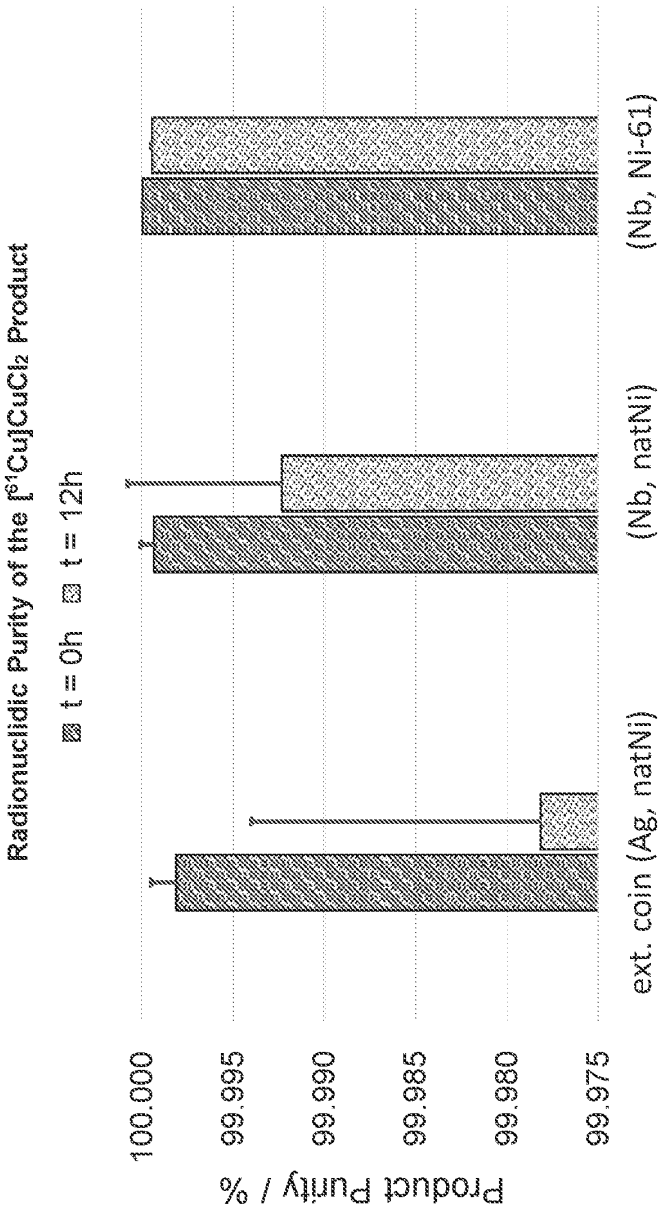

Radionuclidic Purity of the ^{61}Cu]CuCl$_2$ Product
t = 0h
t = 12h
Product Purity / %
100.000
99.995
99.990
99.985
99.980
99.975
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 7

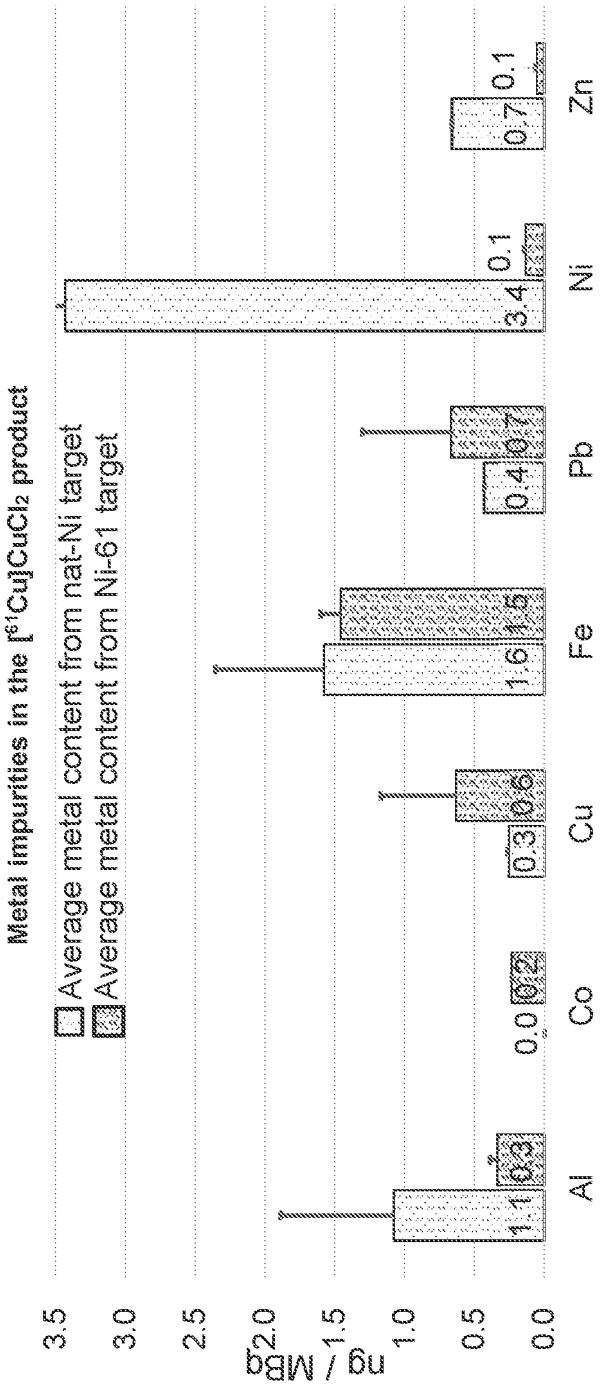

Metal impurities in the [61Cu]CuCl2 product
Average metal content from nat-Ni target
Average metal content from Ni-61 target
ng / MBq
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Al
Co
Cu
Fe
Pb
Ni
Zn
1.1
0.3
0.0
0.2
0.3
0.6
1.6
1.5
0.4
0.7
3.4
0.1
0.7
0.1

FIG. 8

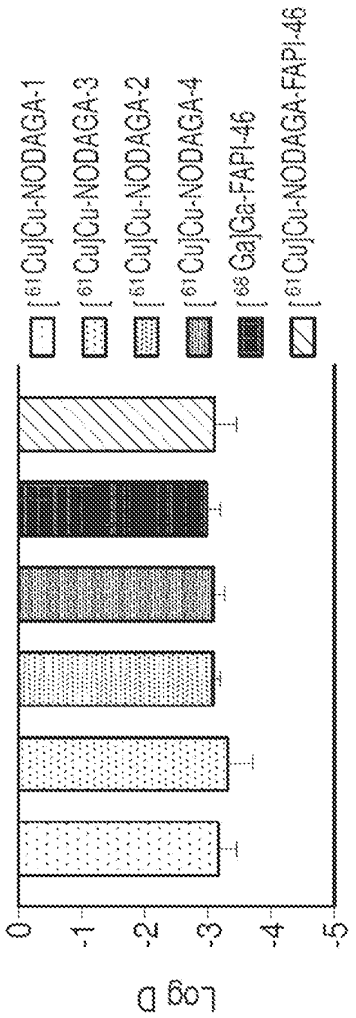

[61Cu]Cu-NODAGA-1
[61Cu]Cu-NODAGA-3
[61Cu]Cu-NODAGA-2
[61Cu]Cu-NODAGA-4
[68Ga]Ga-FAPI-46
[61Cu]Cu-NODAGA-FAPI-46
0
-1
-2
-3
-4
-5
Log D

FIG. 9

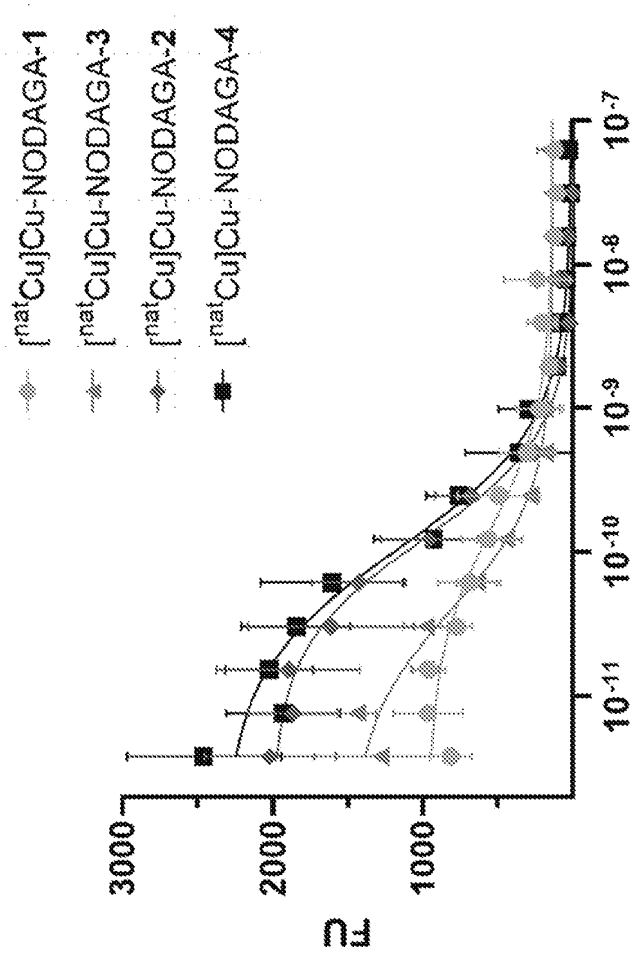

[natCu]Cu-NODAGA-1
[natCu]Cu-NODAGA-3
[natCu]Cu-NODAGA-2
[natCu]Cu- NODAGA-4
3000
2000
1000
FU
10-11
10-10
10-9
10-8
10-7

FIG. 10

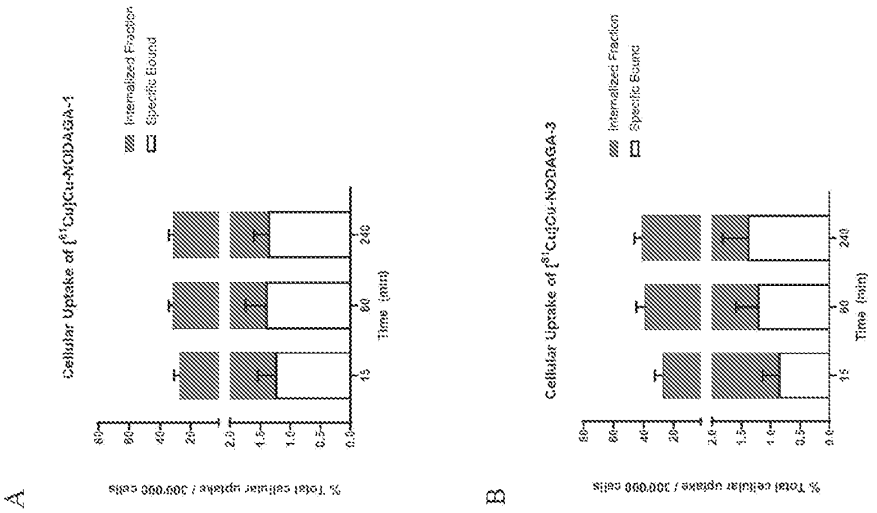
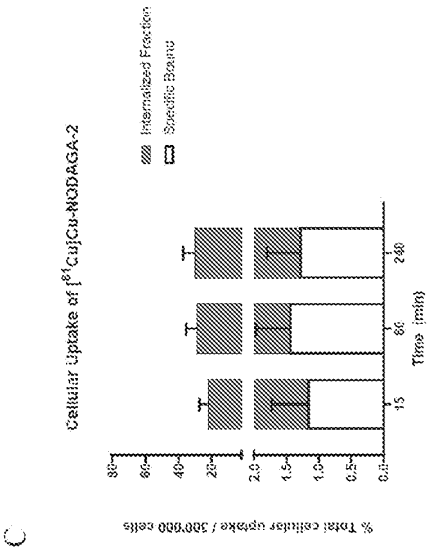

A
Cellular Uptake of [64Cu]Cu-NODAGA-1
Internalized Fraction
Specific Bound
% Total cellular uptake / 300,000 cells
Time (min)
B
Cellular Uptake of [64Cu]Cu-NODAGA-3
Internalized Fraction
Specific Bound
% Total cellular uptake / 300,000 cells
Time (min)

FIG. 11


C
Cellular Uptake of [64Cu]Cu-NODAGA-2
Internalized Fraction
Specific Bound
% Total cellular uptake / 300'000 cells
Time (min)
80
60
40
20
2.0
1.5
1.0
0.5
15
60
240

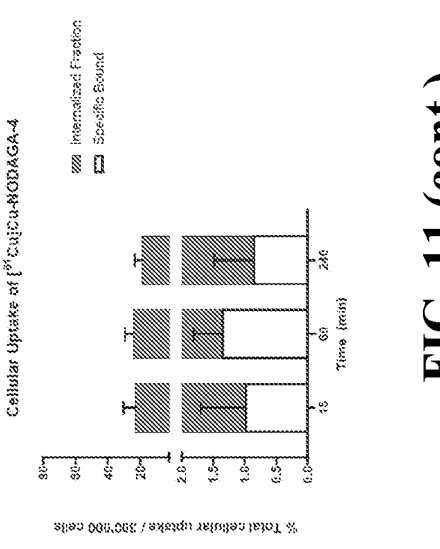

D
Cellular Uptake of [64Cu]Cu-NODAGA-4
Internalized Fraction
Specific Bound
% Total cellular uptake / 300'000 cells
Time (min)
80
60
40
20
2.0
1.5
1.0
0.5
15
60
240

FIG. 11 (cont.)

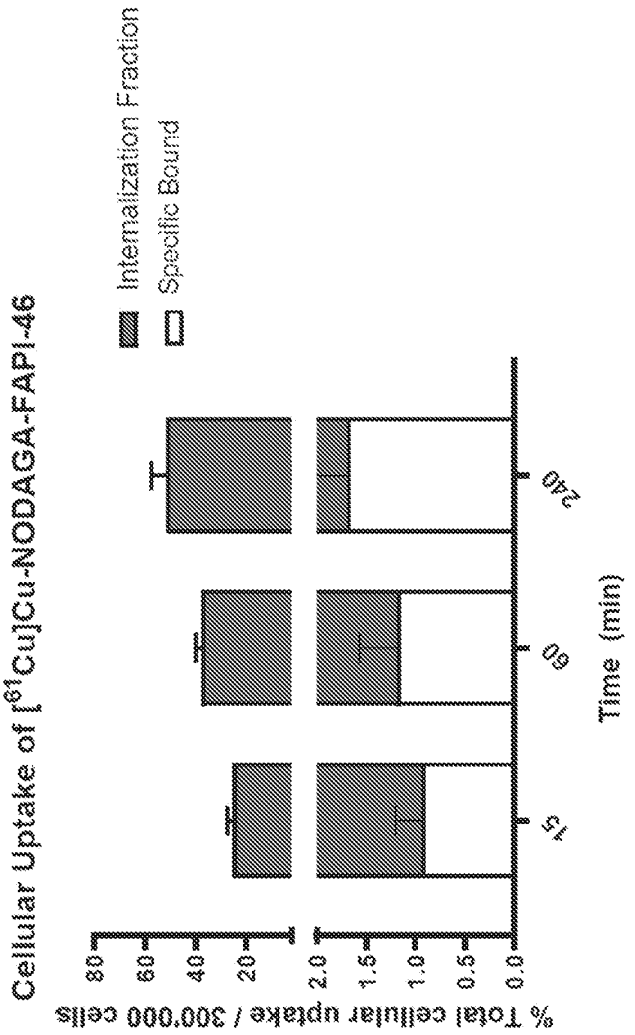

Cellular Uptake of [61Cu]Cu-NODAGA-FAPI-46
Internalization Fraction
Specific Bound
% Total cellular uptake / 300'000 cells
80
60
40
20
2.0
1.5
1.0
0.5
0.0
15
60
240
Time (min)

FIG. 12

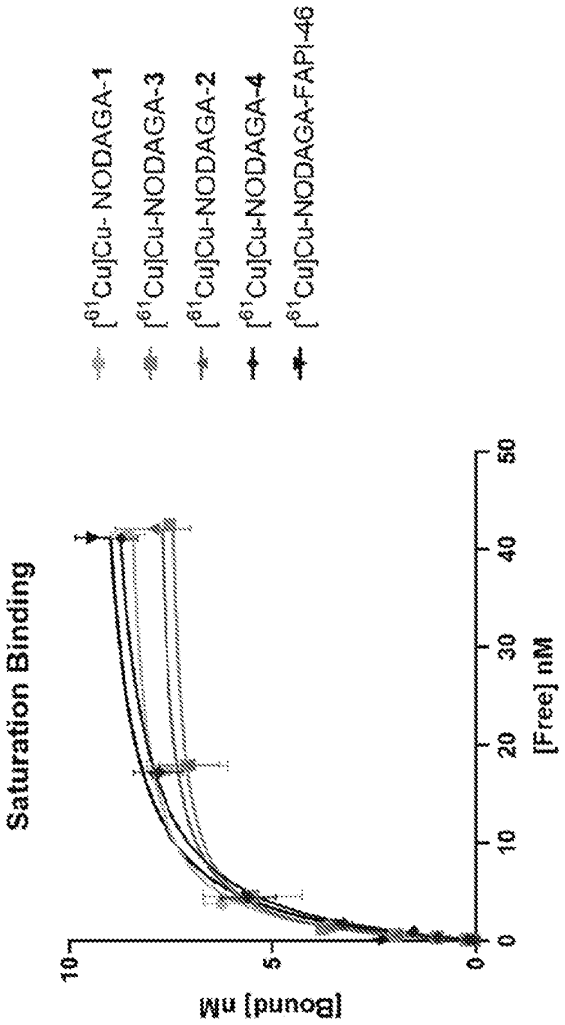

Saturation Binding
[Bound] nM
10
5
0
0
10
20
30
40
50
[Free] nM
[61Cu]Cu- NODAGA-1
[61Cu]Cu-NODAGA-3
[61Cu]Cu-NODAGA-2
[61Cu]Cu-NODAGA-4
[61Cu]Cu-NODAGA-FAPI-46

FIG. 13

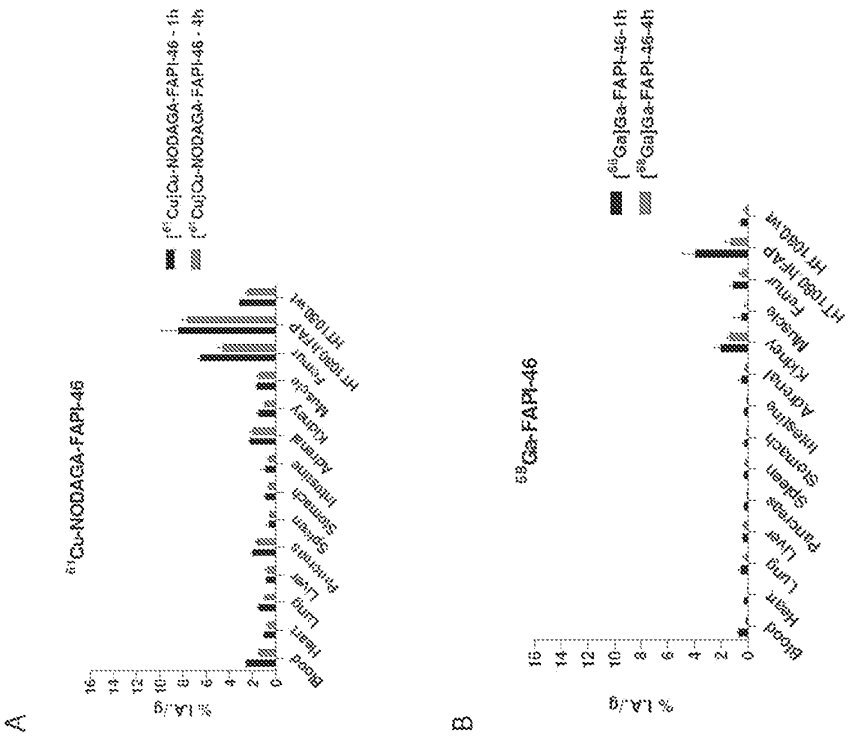

A
^{61}Cu-NODAGA-FAPI-46
[^{61}Cu]Cu-NODAGA-FAPI-46 - 1h
[^{61}Cu]Cu-NODAGA-FAPI-46 - 4h
%IA/g
Blood
Heart
Lung
Liver
Pancreas
Spleen
Stomach
Intestine
Adrenal
Kidney
Muscle
Femur
HT1080 hFAP
HT1080 wt
B
^{68}Ga-FAPI-46
[^{68}Ga]Ga-FAPI-46-1h
[^{68}Ga]Ga-FAPI-46-4h
%IA/g
Blood
Heart
Lung
Liver
Pancreas
Spleen
Stomach
Intestine
Adrenal
Kidney
Muscle
Femur
HT1080 hFAP
HT1080 wt

FIG. 14

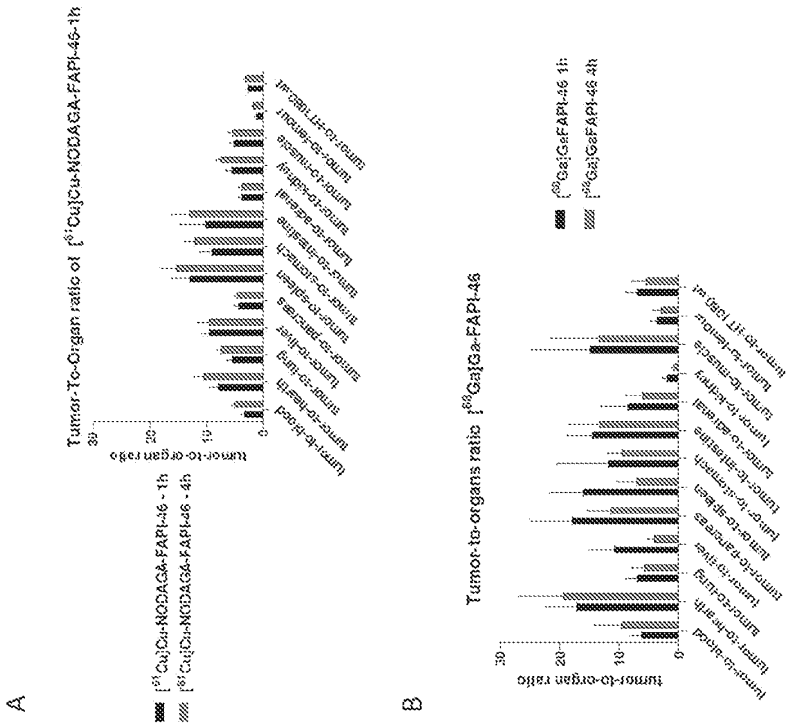

A
Tumor-To-Organ ratio of [64Cu]Cu-NODAGA-FAPI-46-1h
Tumor-to-organ ratio
30
20
10
0
[64Cu]Cu-NODAGA-FAPI-46 - 1h
[64Cu]Cu-NODAGA-FAPI-46 - 4h
Tumor-to-blood
Tumor-to-heart
Tumor-to-lung
Tumor-to-liver
Tumor-to-kidneys
Tumor-to-spleen
Tumor-to-muscle
Tumor-to-stomach
Tumor-to-small intestine
Tumor-to-large intestine
Tumor-to-pancreas
Tumor-to-adrenal
Tumor-to-bone
Tumor-to-brain
B
Tumor-to-organs ratio [68Ga]Ga-FAPI-46
Tumor-to-organ ratio
30
20
10
0
[68Ga]GaFAPI-46 1h
[68Ga]GaFAPI-46 4h
Tumor-to-blood
Tumor-to-heart
Tumor-to-lung
Tumor-to-liver
Tumor-to-kidneys
Tumor-to-spleen
Tumor-to-muscle
Tumor-to-stomach
Tumor-to-small intestine
Tumor-to-large intestine
Tumor-to-pancreas
Tumor-to-adrenal
Tumor-to-bone
Tumor-to-brain

FIG. 15

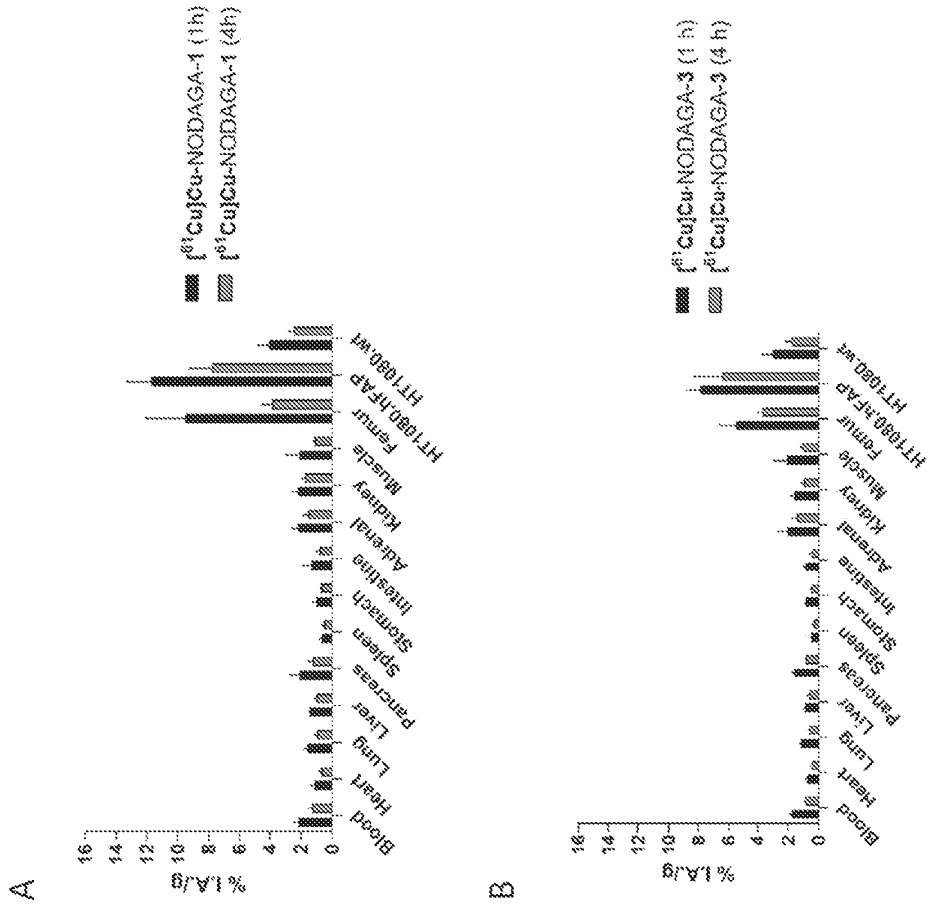

A
[61Cu]Cu-NODAGA-1 (1h)
[61Cu]Cu-NODAGA-1 (4h)
%IA/g
0
2
4
6
8
10
12
14
16
Blood
Heart
Lung
Liver
Pancreas
Spleen
Stomach
Intestine
Adrenal
Kidney
Muscle
Femur
HT1080.hFAP
HT1080.wt
B
[61Cu]Cu-NODAGA-3 (1 h)
[61Cu]Cu-NODAGA-3 (4 h)
%IA/g
0
2
4
6
8
10
12
14
16
Blood
Heart
Lung
Liver
Pancreas
Spleen
Stomach
Intestine
Adrenal
Kidney
Muscle
Femur
HT1080.hFAP
HT1080.wt

FIG. 16

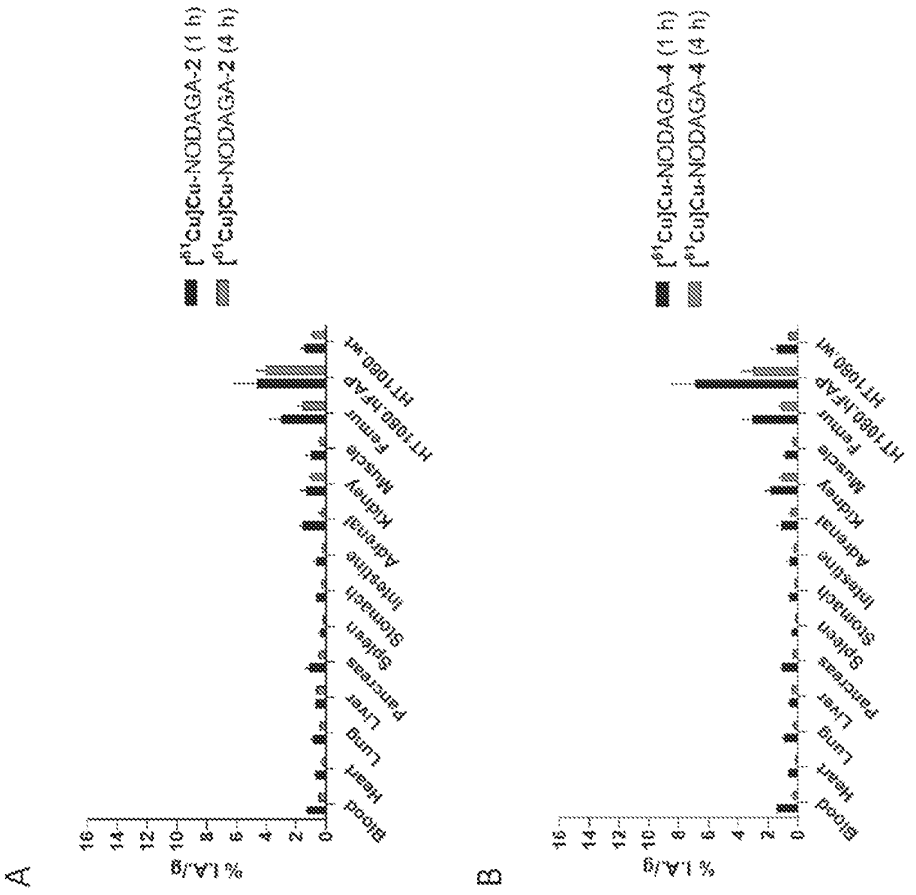

A
B
% I.A./g
Blood
Heart
Lung
Liver
Pancreas
Spleen
Stomach
Intestine
Adrenal
Kidney
Muscle
Femur
HT1080.hFAP
HT1080.wt

FIG. 17

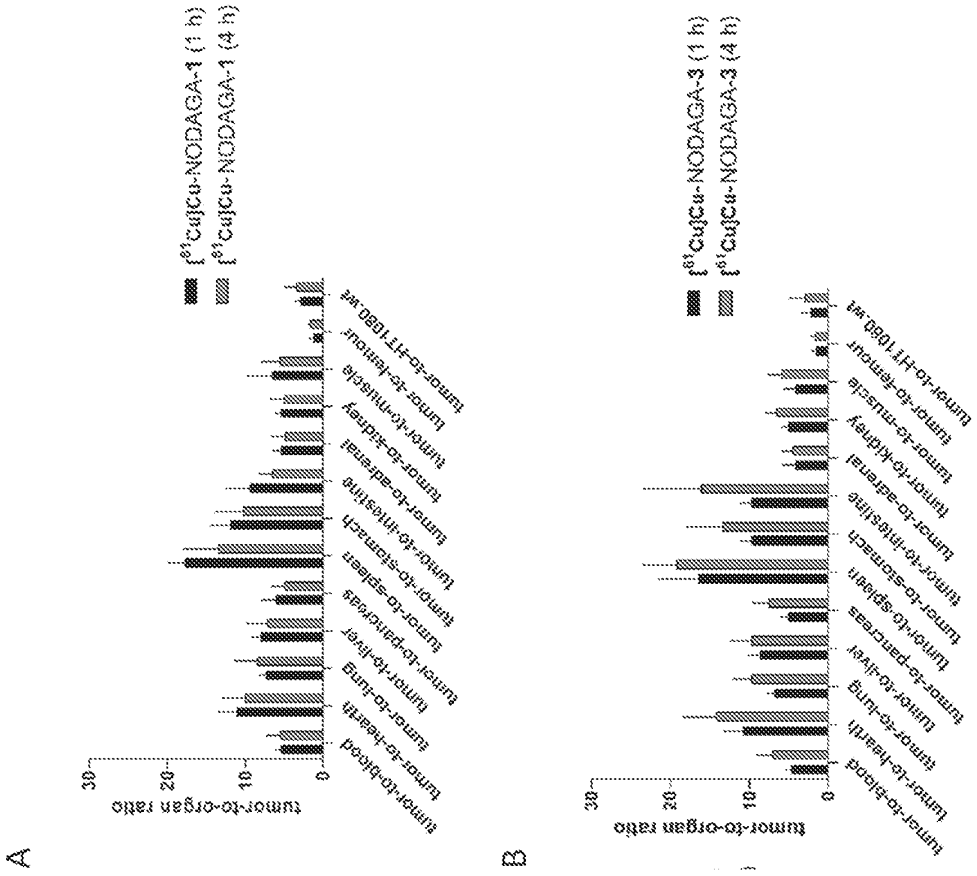

A
B
tumor-to-organ ratio
30
20
10
0
[61Cu]Cu-NODAGA-1 (1 h)
[61Cu]Cu-NODAGA-1 (4 h)
[61Cu]Cu-NODAGA-3 (1 h)
[61Cu]Cu-NODAGA-3 (4 h)
tumor-to-blood
tumor-to-heart
tumor-to-lung
tumor-to-liver
tumor-to-pancreas
tumor-to-spleen
tumor-to-stomach
tumor-to-intestine
tumor-to-adrenal
tumor-to-kidney
tumor-to-muscle
tumor-to-femur
tumor-to-HT1080.wt

FIG. 18

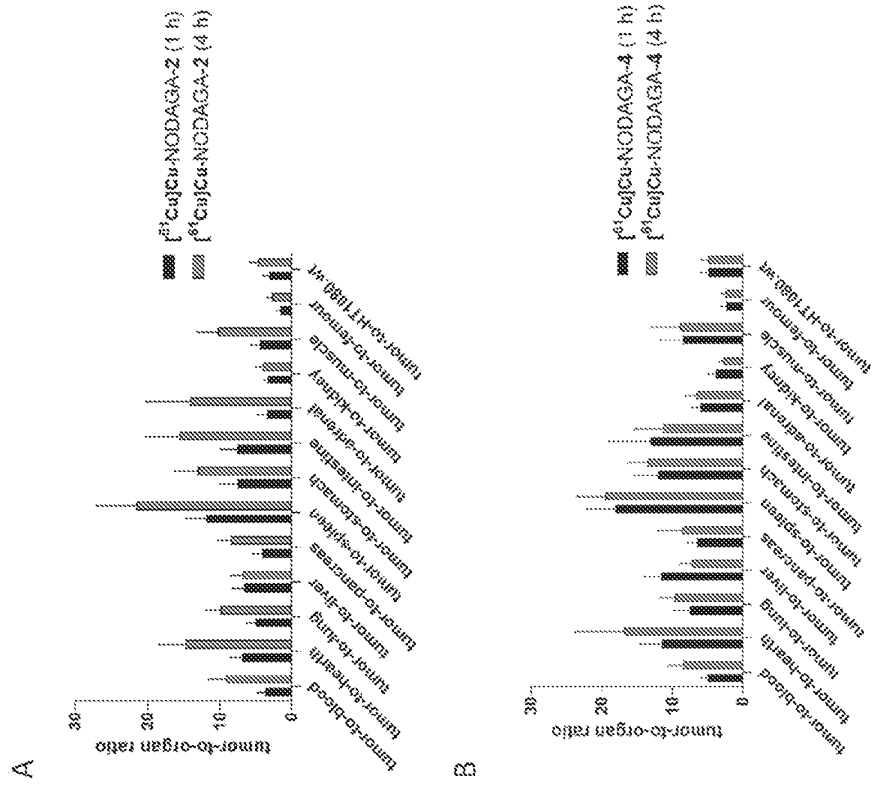

A
[64Cu]Cu-NODAGA-2 (1 h)
[64Cu]Cu-NODAGA-2 (4 h)
tumor-to-organ ratio
0
10
20
30
tumor-to-blood
tumor-to-heart
tumor-to-lung
tumor-to-liver
tumor-to-pancreas
tumor-to-spleen
tumor-to-stomach
tumor-to-intestine
tumor-to-adrenal
tumor-to-kidney
tumor-to-muscle
tumor-to-femour
tumor-to-HT1080-wt
B
[61Cu]Cu-NODAGA-4 (1 h)
[61Cu]Cu-NODAGA-4 (4 h)
tumor-to-organ ratio
0
10
20
30
tumor-to-blood
tumor-to-heart
tumor-to-lung
tumor-to-liver
tumor-to-pancreas
tumor-to-spleen
tumor-to-stomach
tumor-to-intestine
tumor-to-adrenal
tumor-to-kidney
tumor-to-muscle
tumor-to-femour
tumor-to-HT1080-wt

FIG. 19

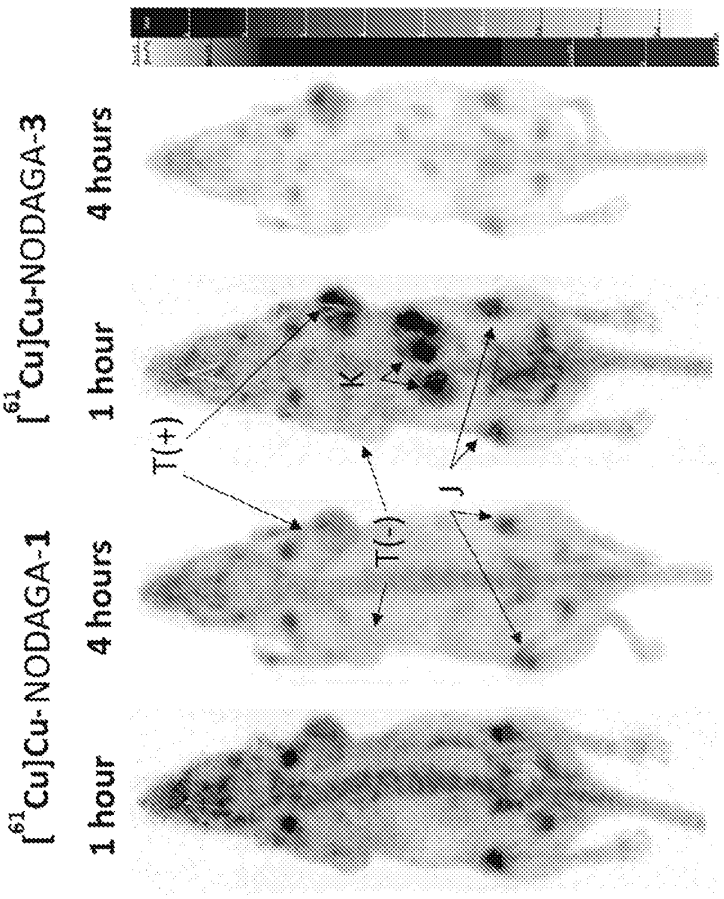

[61Cu]Cu-NODAGA-1
1 hour
4 hours
[61Cu]Cu-NODAGA-3
1 hour
4 hours
T(+)
T(-)
K
J

FIG. 20

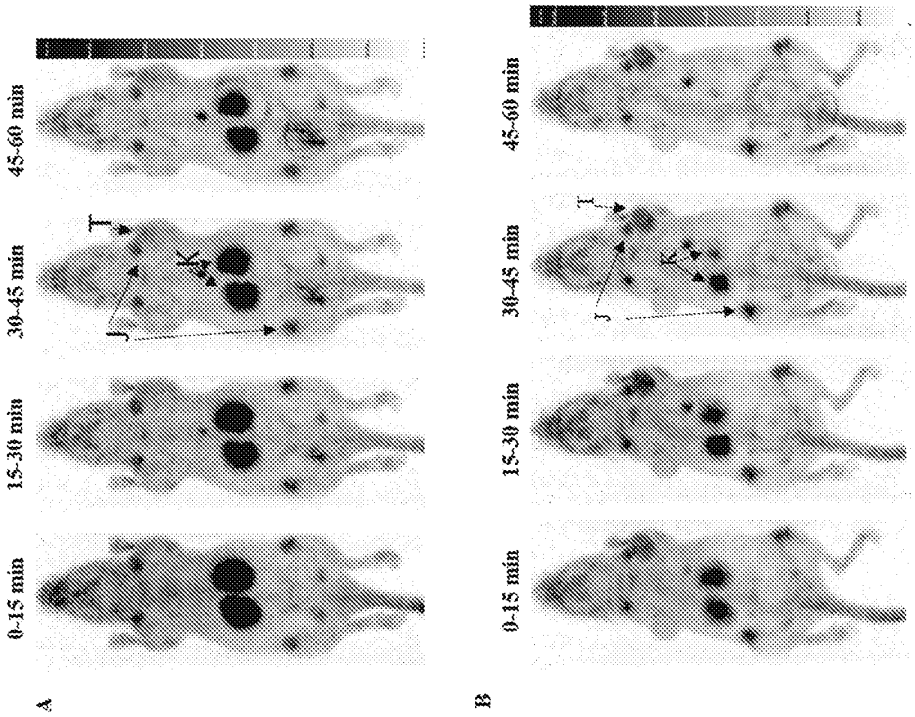

A
0-15 min
15-30 min
30-45 min
45-60 min
T
K
J
B
0-15 min
15-30 min
30-45 min
45-60 min
T
K
J

FIG. 21

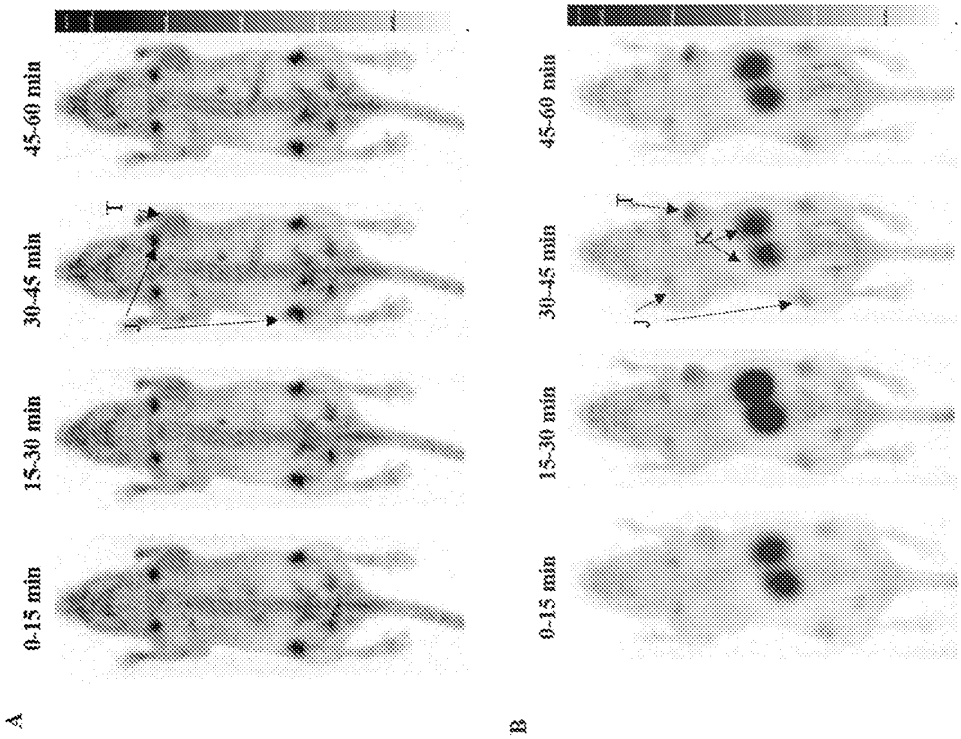

A
0-15 min
15-30 min
30-45 min
45-60 min
T
L
B
0-15 min
15-30 min
30-45 min
45-60 min
T
K
J

FIG. 22

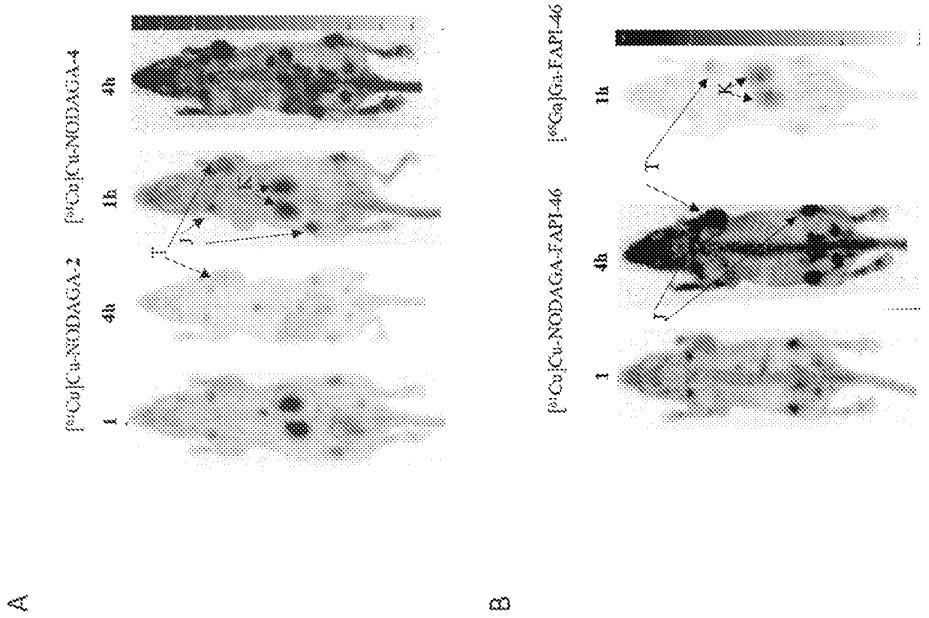

A
[68Ga]Ga-NODAGA-2
[68Ga]Ga-NODAGA-4
1h
4h
T
J
B
[68Ga]Ga-NODAGA-FAPI-46
[68Ga]Ga-FAPI-46
K

FIG. 23

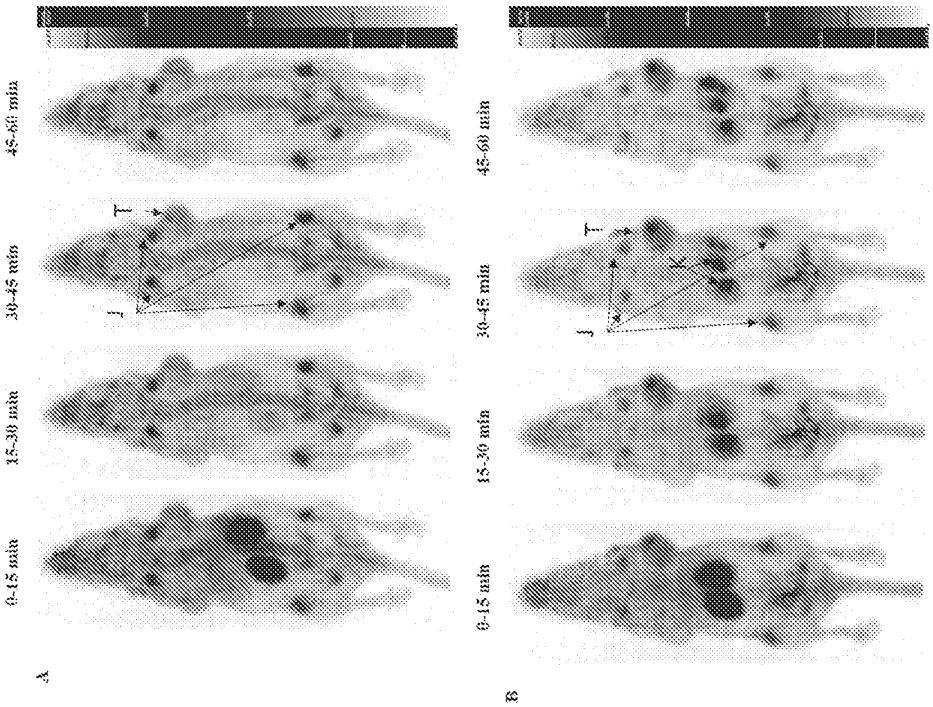


FIG. 24