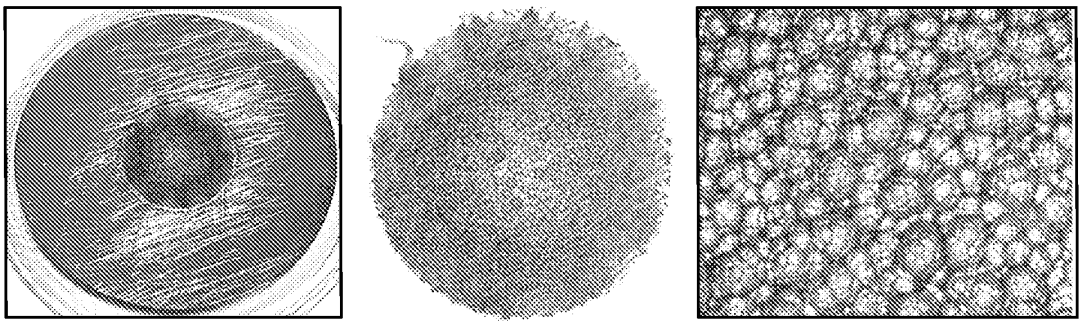


FIG. 1

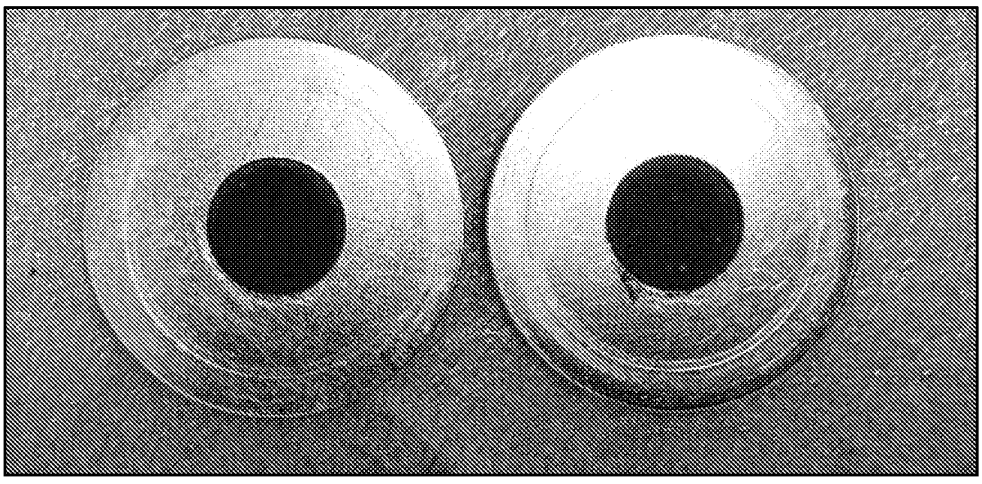


FIG. 2

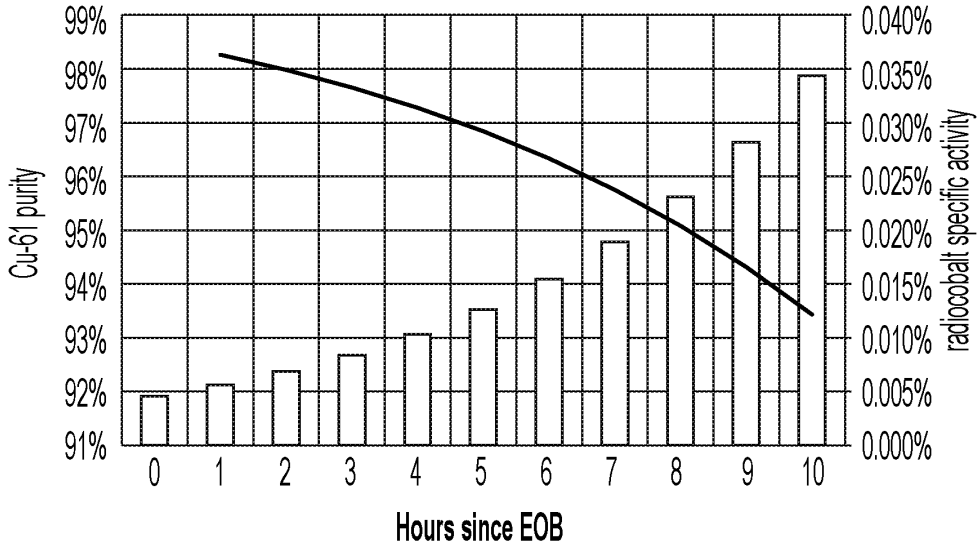

99%
98%
97%
96%
95%
94%
93%
92%
91%
Cu-61 purity
0.040%
0.035%
0.030%
0.025%
0.020%
0.015%
0.010%
0.005%
0.000%
radiocobalt specific activity
0 1 2 3 4 5 6 7 8 9 10
Hours since EOB

FIG. 3

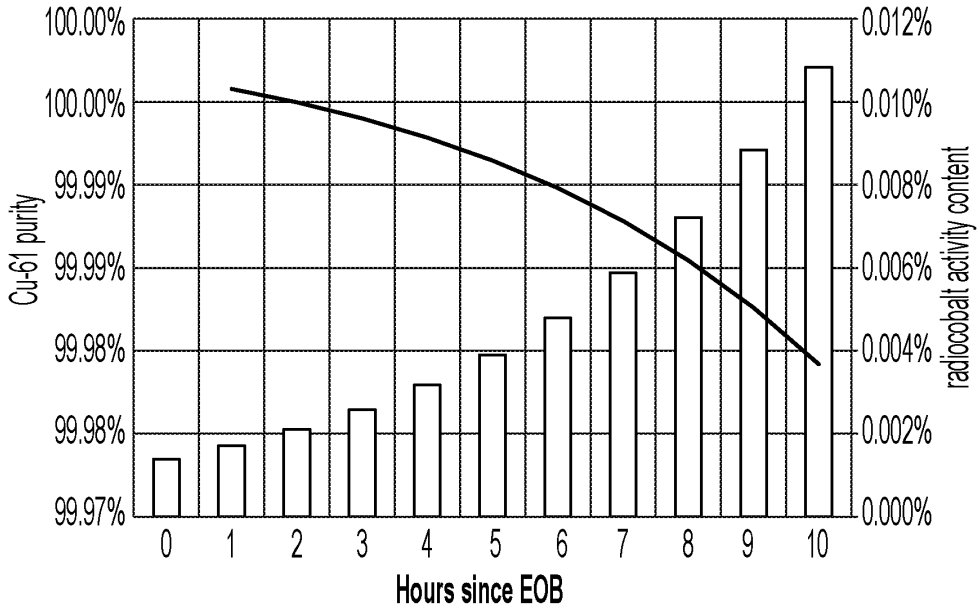

100.00%
100.00%
99.99%
99.99%
99.98%
99.98%
99.97%
Cu-61 purity
0.012%
0.010%
0.008%
0.006%
0.004%
0.002%
0.000%
radiocobalt activity content
0 1 2 3 4 5 6 7 8 9 10
Hours since EOB

FIG. 4

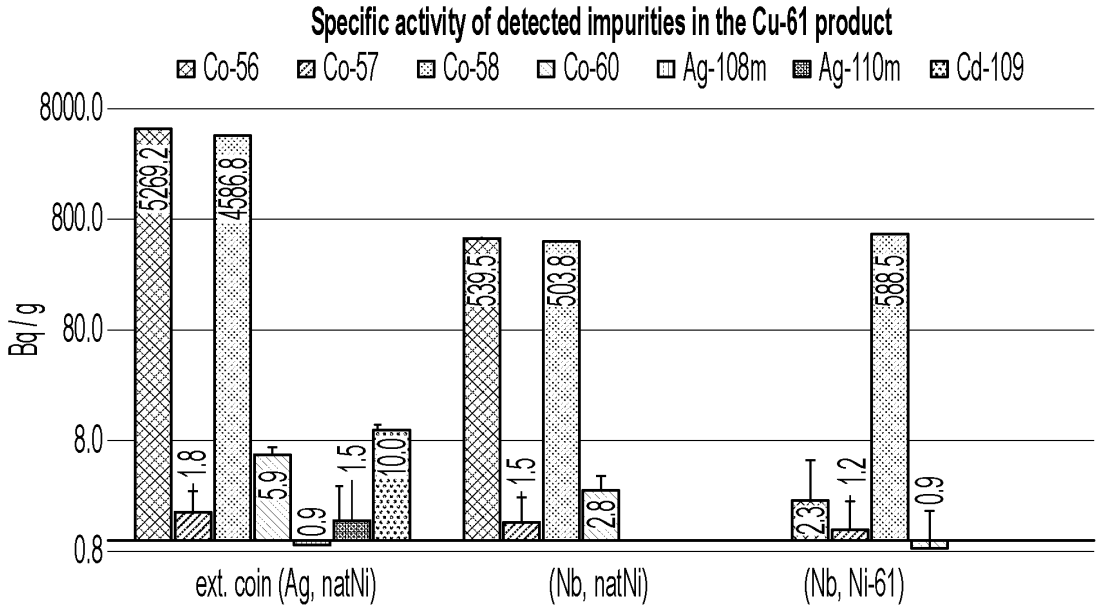

Specific activity of detected impurities in the Cu-61 product
Co-56
Co-57
Co-58
Co-60
Ag-108m
Ag-110m
Cd-109
8000.0
800.0
80.0
8.0
0.8
Bq / g
5269.2
1.8
4586.8
5.9
0.9
1.5
10.0
539.5
1.5
503.8
2.8
2.3
1.2
588.5
0.9
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 5

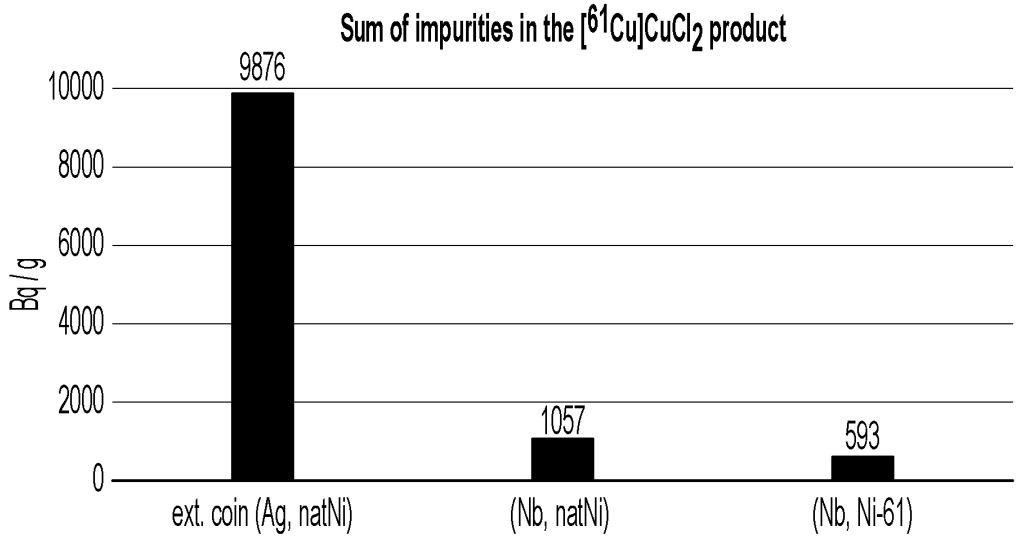

Sum of impurities in the [61Cu]CuCl2 product
10000
8000
6000
4000
2000
0
Bq / g
9876
1057
593
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 6

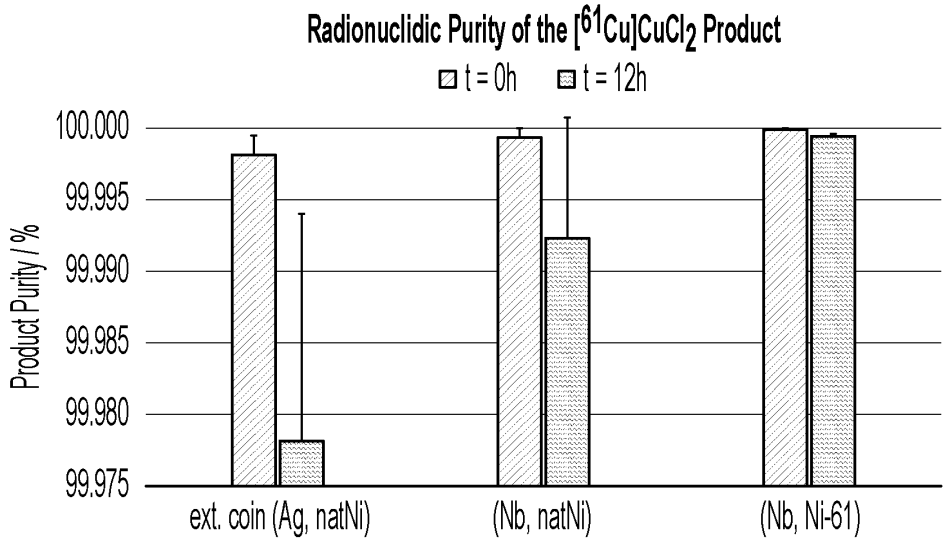

Radionuclidic Purity of the [61Cu]CuCl2 Product
t = 0h
t = 12h
Product Purity / %
100.000
99.995
99.990
99.985
99.980
99.975
ext. coin (Ag, natNi)
(Nb, natNi)
(Nb, Ni-61)

FIG. 7

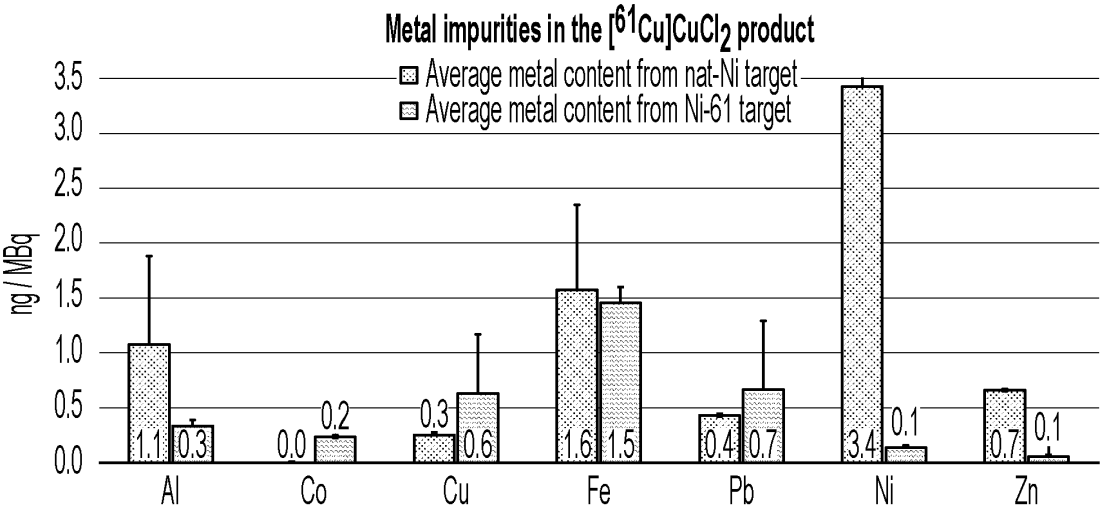

Metal impurities in the [61Cu]CuCl2 product
Average metal content from nat-Ni target
Average metal content from Ni-61 target
ng / MBq
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.1
0.3
0.0
0.2
0.3
0.6
1.6
1.5
0.4
0.7
3.4
0.1
0.7
0.1
Al
Co
Cu
Fe
Pb
Ni
Zn

FIG. 8

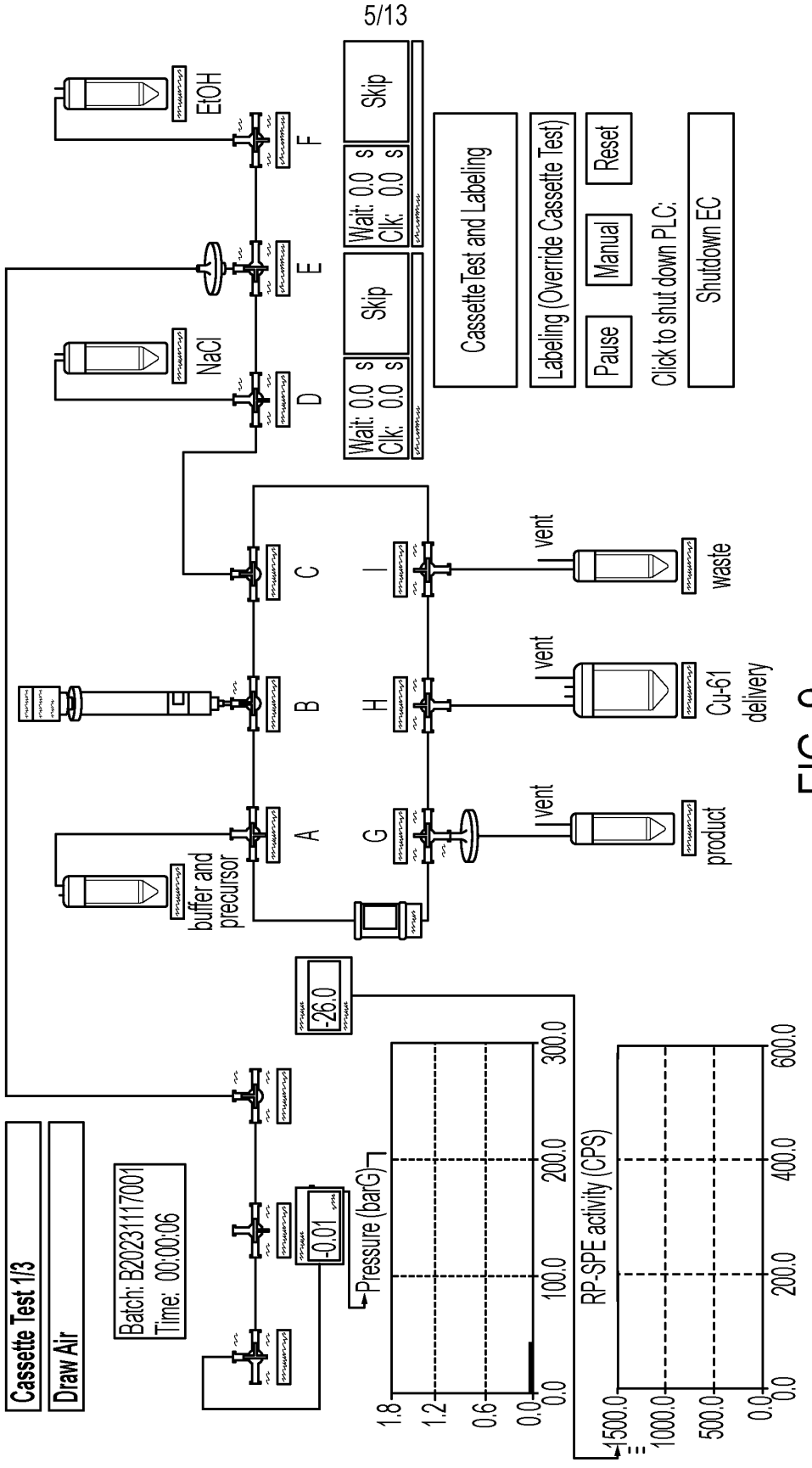

Cassette Test 1/3
Draw Air
Batch: B2023117001
Time: 00:00:06
-0.01
-26.0
Pressure (barG)
1.8
1.2
0.6
0.0
0.0
100.0
200.0
300.0
RP-SPE activity (CPS)
1500.0
1000.0
500.0
0.0
0.0
200.0
400.0
600.0
buffer and precursor
A
B
C
D
NaCl
E
F
EtOH
G
H
I
vent
waste
vent
Cu-61 delivery
vent
product
Wait: 0.0 s
Clk: 0.0 s
Skip
Wait: 0.0 s
Clk: 0.0 s
Skip
Cassette Test and Labeling
Labeling (Override Cassette Test)
Pause
Manual
Reset
Click to shut down PLC:
Shutdown EC

FIG. 9

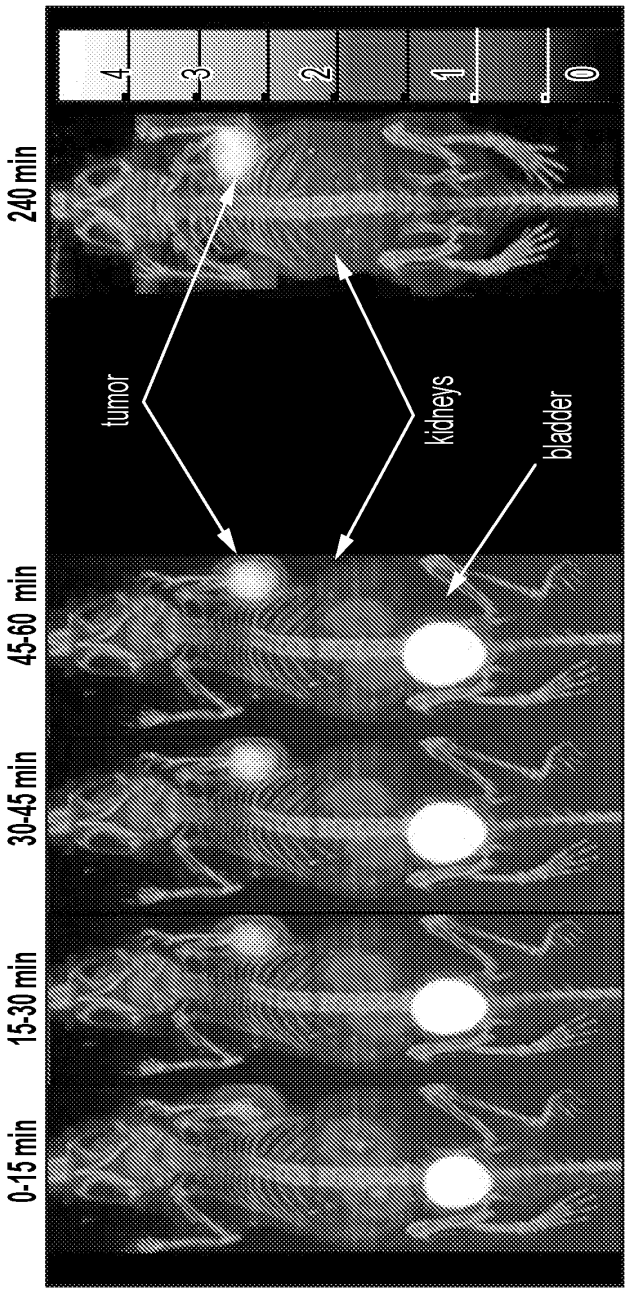

4
3
2
1
0
240 min
45-60 min
30-45 min
15-30 min
0-15 min
tumor
kidneys
bladder

FIG. 10

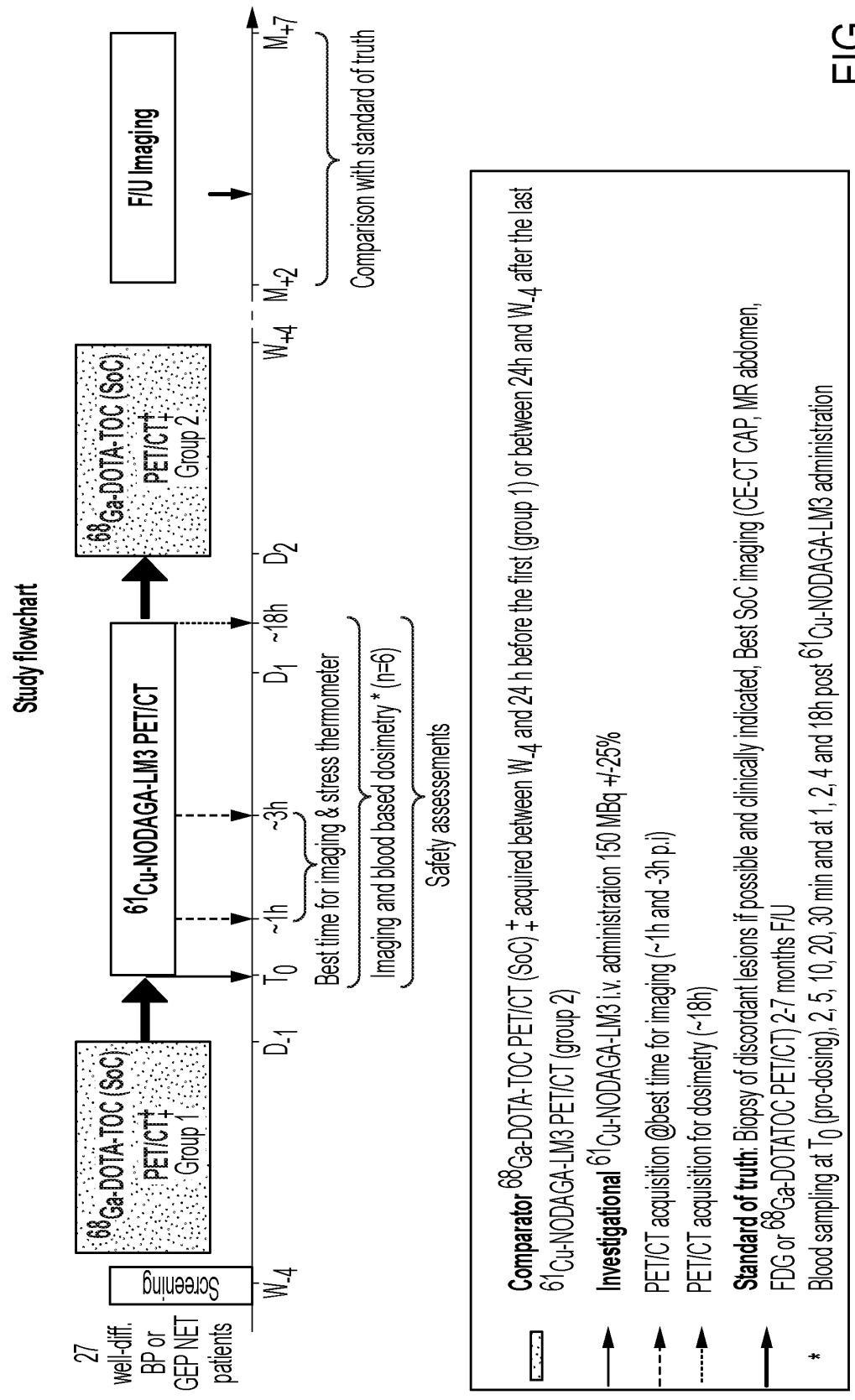

Study flowchart
27 well-diff. BP or GEP NET patients
Screening
W-4
68Ga-DOTA-TOC (SoC) PET/CT± Group 1
61Cu-NODAGA-LM3 PET/CT
D-1
T0
~1h
~3h
D1
~18h
D2
68Ga-DOTA-TOC (SoC) PET/CT± Group 2
W+4
M+2
F/U Imaging
M+7
Best time for imaging & stress thermometer
Imaging and blood based dosimetry * (n=6)
Safety assessements
Comparison with standard of truth
Comparator 68Ga-DOTA-TOC PET/CT (SoC) ± acquired between W-4 and 24 h before the first (group 1) or between 24h and W-4 after the last 61Cu-NODAGA-LM3 PET/CT (group 2)
Investigational 61Cu-NODAGA-LM3 i.v. administration 150 MBq +/-25%
PET/CT acquisition @best time for imaging (~1h and -3h p.i)
PET/CT acquisition for dosimetry (~18h)
Standard of truth: Biopsy of discordant lesions if possible and clinically indicated, Best SoC imaging (CE-CT CAP, MR abdomen, FDG or 68Ga-DOTATOC PET/CT) 2-7 months F/U
* Blood sampling at T0 (pro-dosing), 2, 5, 10, 20, 30 min and at 1, 2, 4 and 18h post 61Cu-NODAGA-LM3 administration

FIG. 11

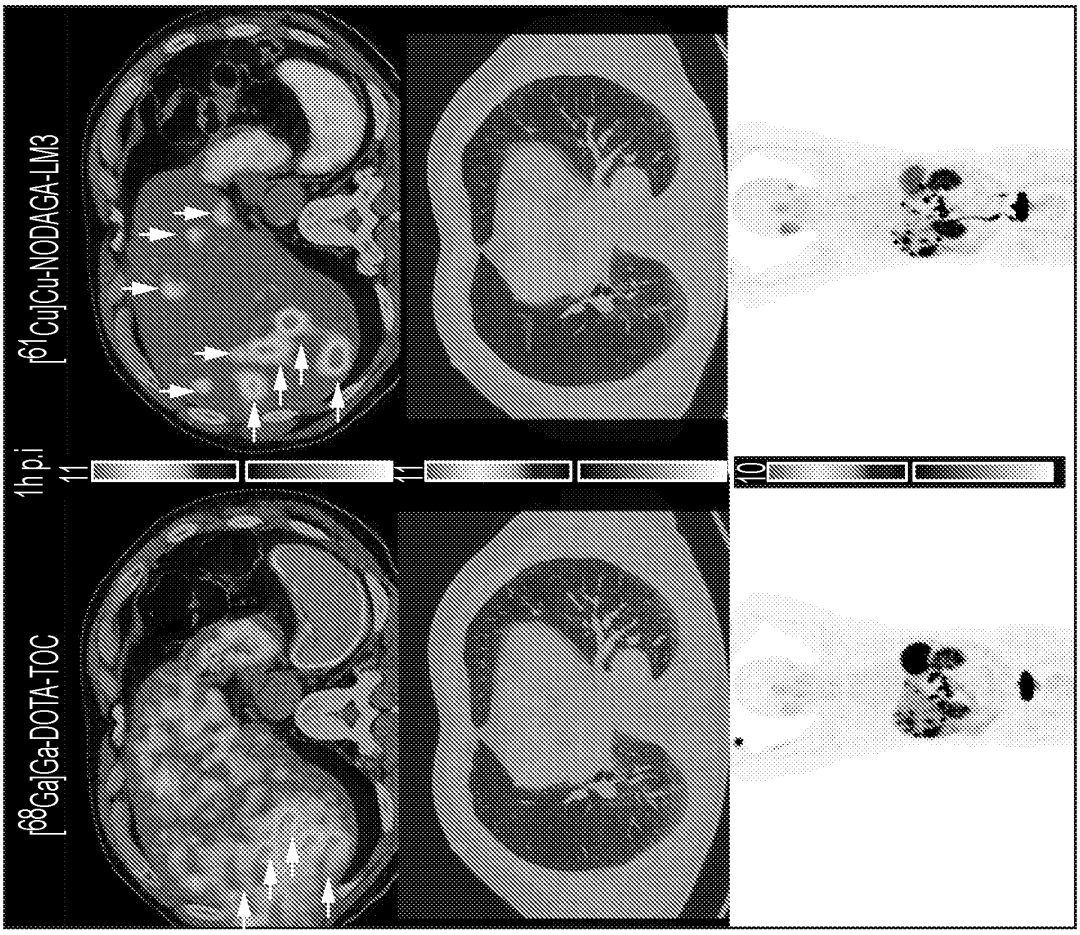
9.1 Table of study procedures and assessments / Study schedule

Visit name	Screening	^{61}Cu-NODAGA-LM3 PET/CT (Visit 1)	^{61}Cu-NODAGA-LM3 PET/CT (Visit 2)	Follow up visit
Visit schedule	max. 4 weeks before visit 2	max. +/-4 weeks to SoC Ga-TOC PET/CT	1 day after IMP administration	~2 - 7 months after visit 2
Consent	X			
^{61}Cu-LM3 PET/CT before or after SoC ^{68}Ga-TOC PET/CT (clinical randomization)	X			
Past medical/ surgical NET and non-NET history	X			
Concommitant medications, especially if SSA (form, dose, last time of injection)	X	X		
Baseline NET disease characteristics (primary site, histology, Ki-67 value)	X			
SoC ^{68}Ga-DOTATOC PET/CT at USB max. +/-4 weeks to ^{61}Cu-NODAGA-LM3 PET/CT	X			
NETest	X			
Verification of eligibility criteria	X	X		
Intervention (Injection of ^{61}Cu-NODAGA-LM3)		X		
Whole body PET/CT ~1 p.i		X		
Whole body PET/CT ~3h p.i		X		
Whole body PET/CT ~18h*			X*	
Adverse events (before and after IMP injection)		X	X*	
Vital signs (before and after IMP injection)		X	X*	
Physical examination (before and after IMP injection)		X	X*	
Laboratory (diff. BCC + Chemistry) (before and up to ~4h p.i)	X	X		
β-HCG test in woman in child bearing age		X		
Patient reported stress (stress thermometer); at baseline and ~1h and ~3h p.i.		X		
PK / dosimetry* blood sampling (0, 2, 5, 10, 20, 30 min and ~1, ~2, ~4 and ~18h p.i)		X*	X*	
Follow-up best molecular (^{68}Ga-DOTATOC or FDG PET/CT) and / or morphological imaging (MRI abdomen or CT CAP) with contrast at USB (SoC)				X
Biopsy for histological confirmation (optional; SoC)				X

*Only in a subset of 6 patients.

FIG. 12

FIG. 13



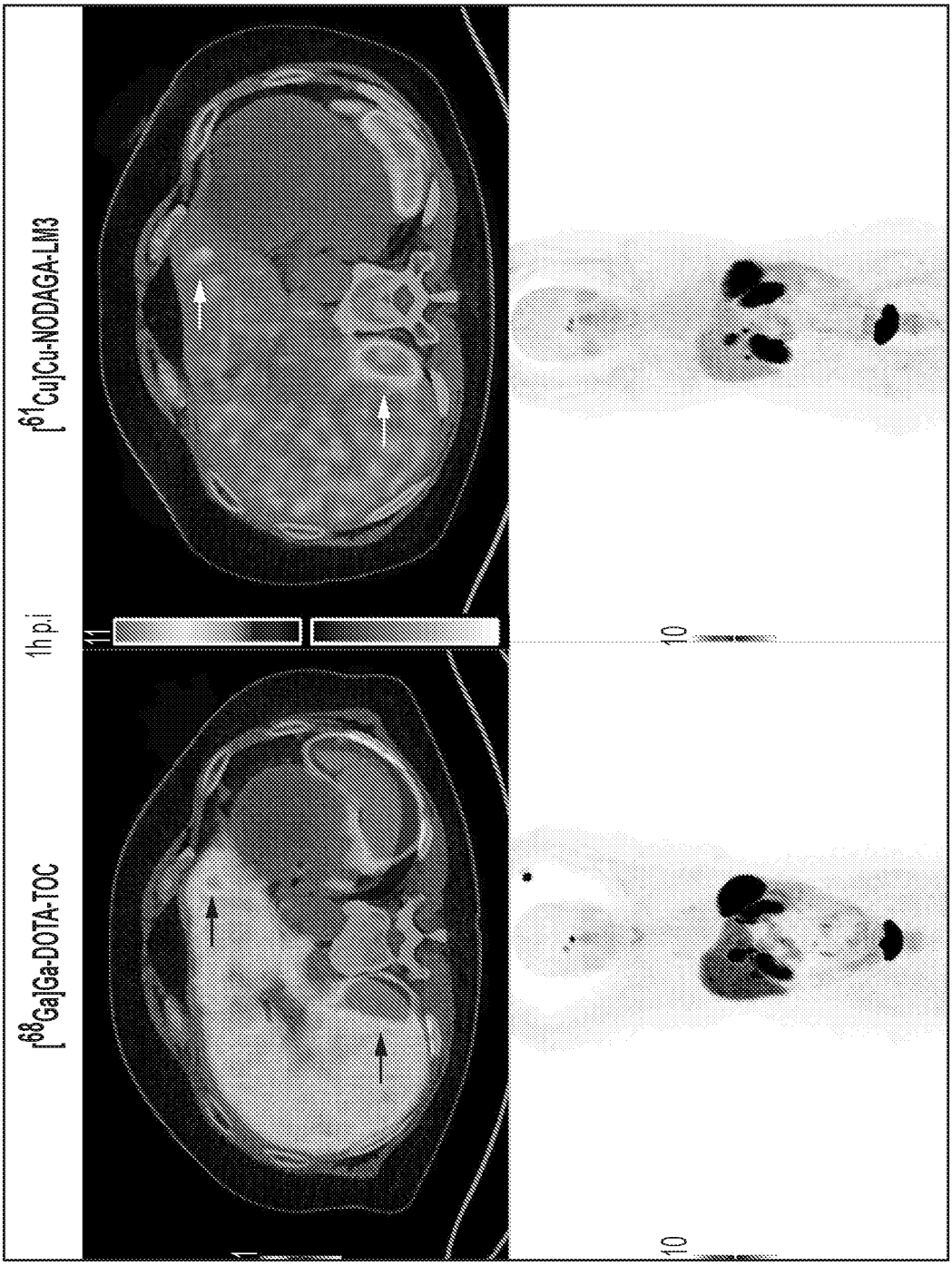
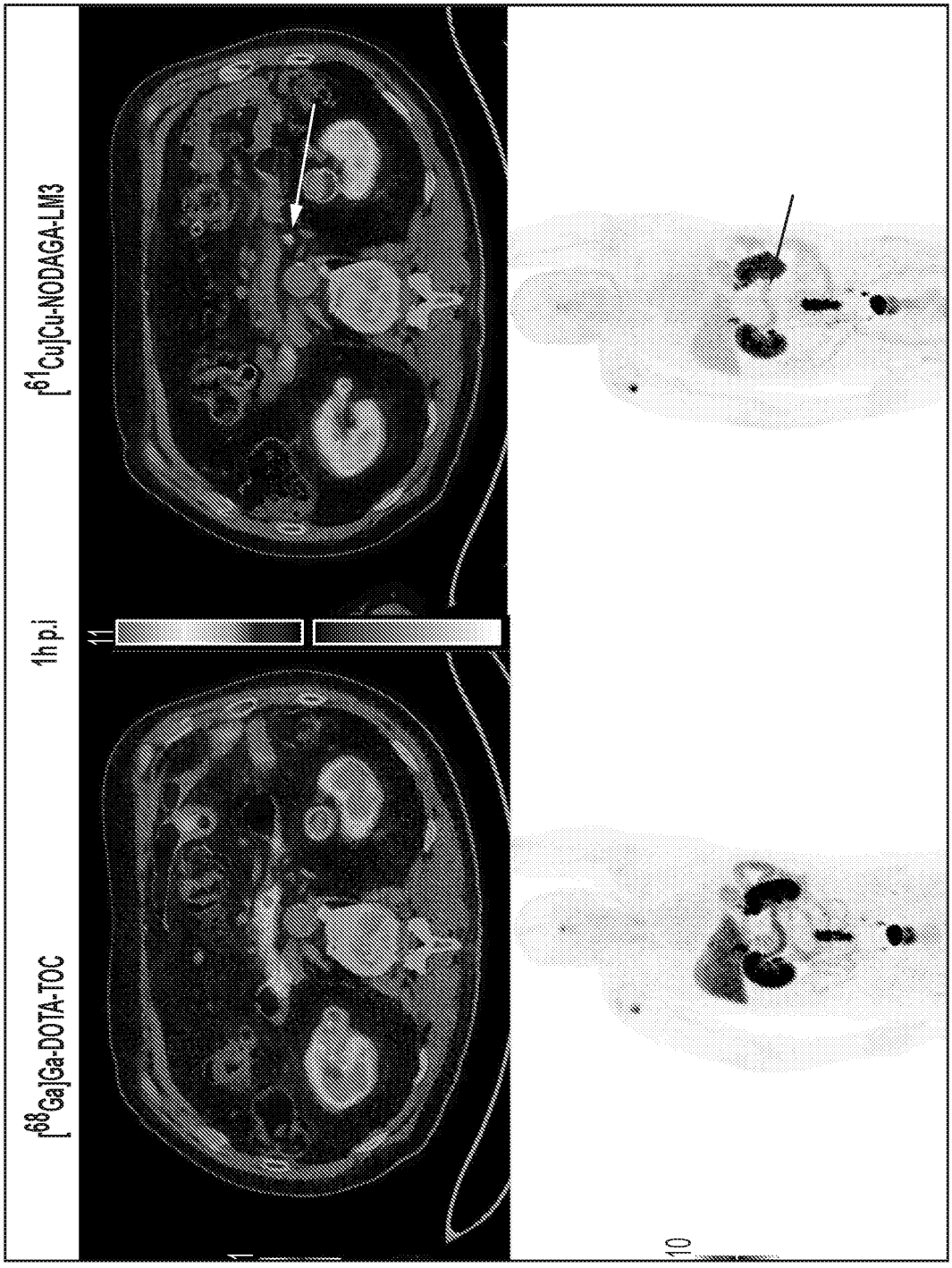


FIG. 14

FIG. 15



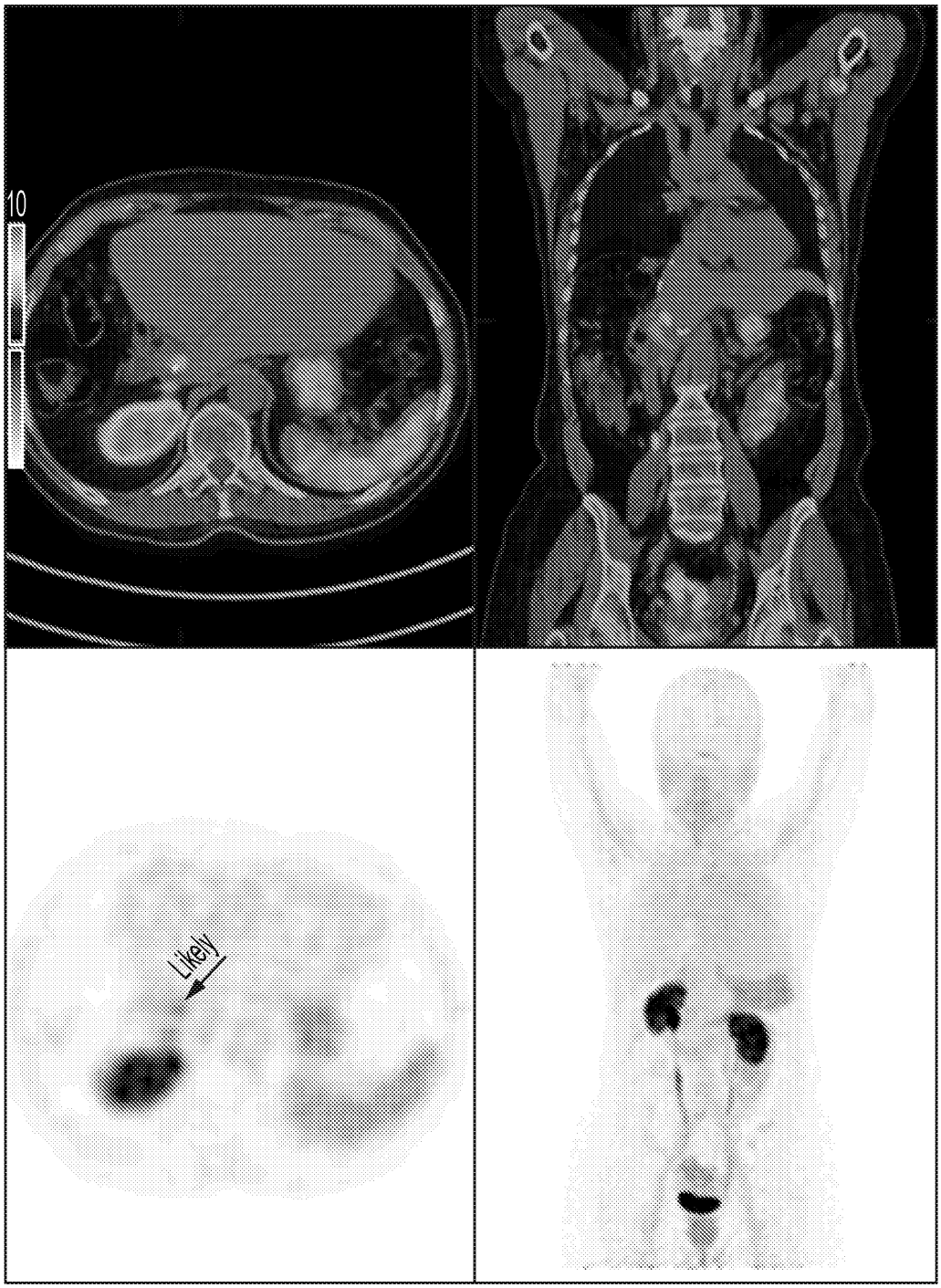


FIG. 16

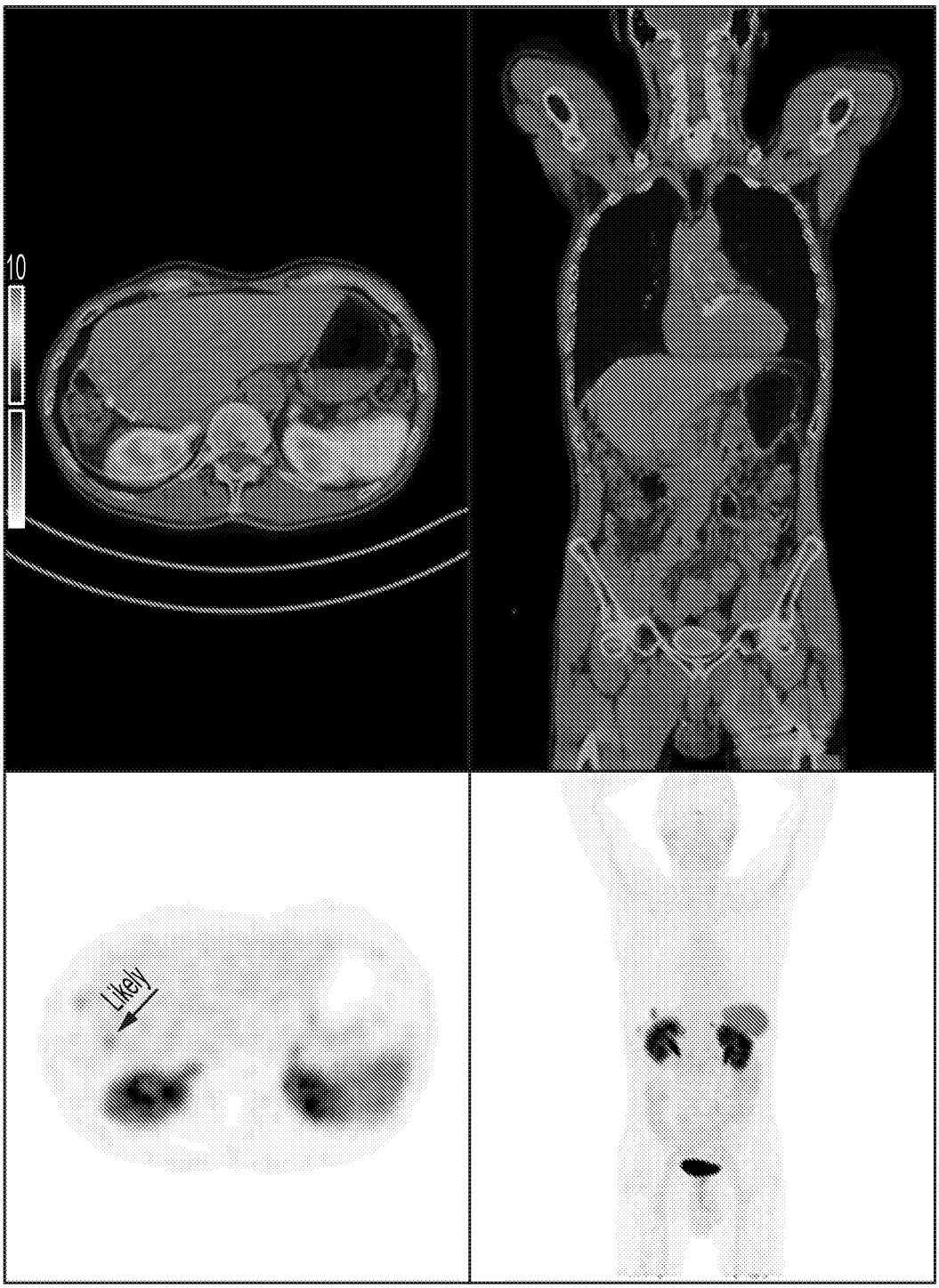


FIG. 17