Fig. 1

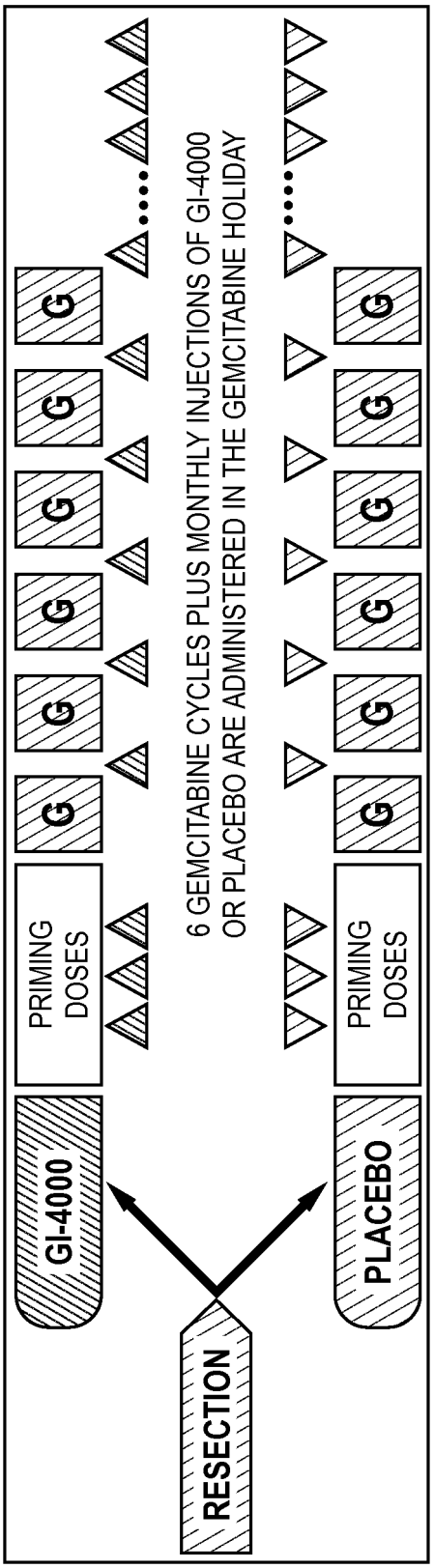

RESECTION
GI-4000
PLACEBO
PRIMING DOSES
PRIMING DOSES
6 GEMCITABINE CYCLES PLUS MONTHLY INJECTIONS OF GI-4000
OR PLACEBO ARE ADMINISTERED IN THE GEMCITABINE HOLIDAY
G

Fig. 2A

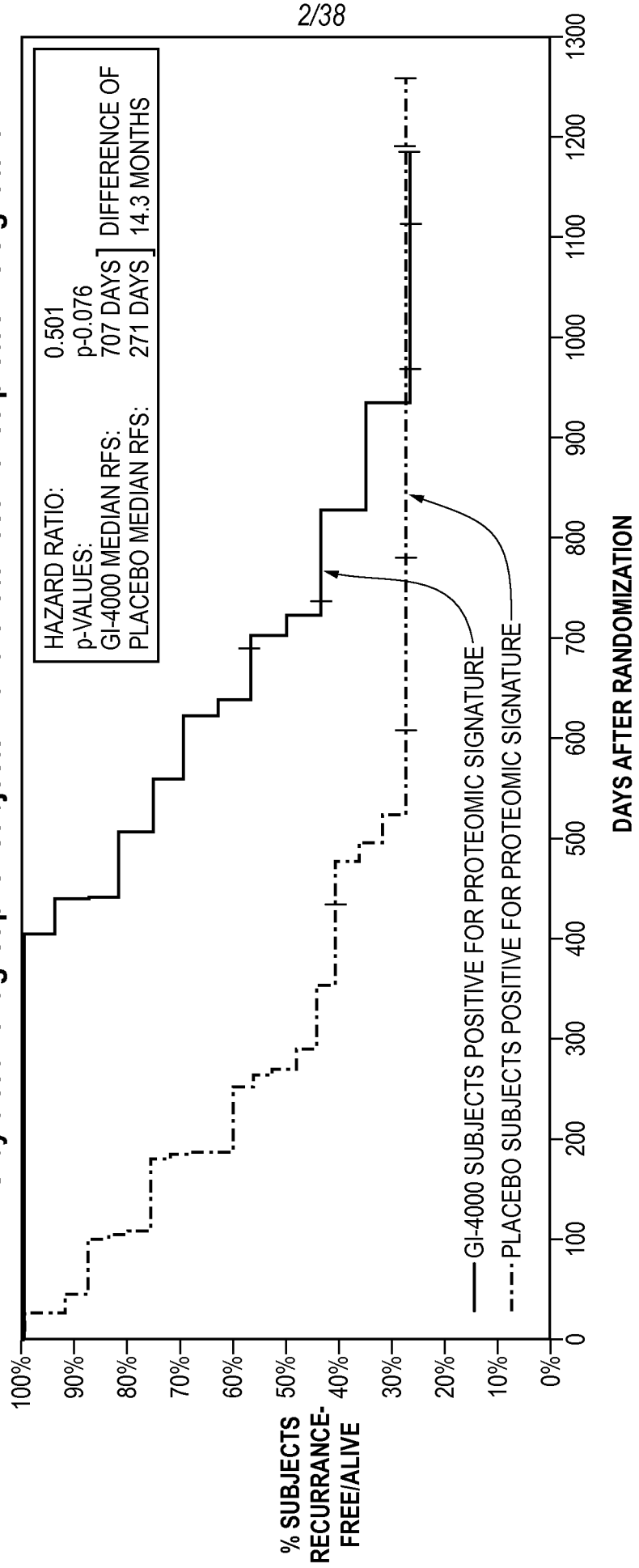

RFS by treatment group for subjects with the late-recurrence proteomic signature
HAZARD RATIO: 0.501
p-VALUES: p-0.076
GI-4000 MEDIAN RFS: 707 DAYS] DIFFERENCE OF
PLACEBO MEDIAN RFS: 271 DAYS] 14.3 MONTHS
GI-4000 SUBJECTS POSITIVE FOR PROTEOMIC SIGNATURE
PLACEBO SUBJECTS POSITIVE FOR PROTEOMIC SIGNATURE
% SUBJECTS RECURRANCE-FREE/ALIVE
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
DAYS AFTER RANDOMIZATION

Fig. 2B

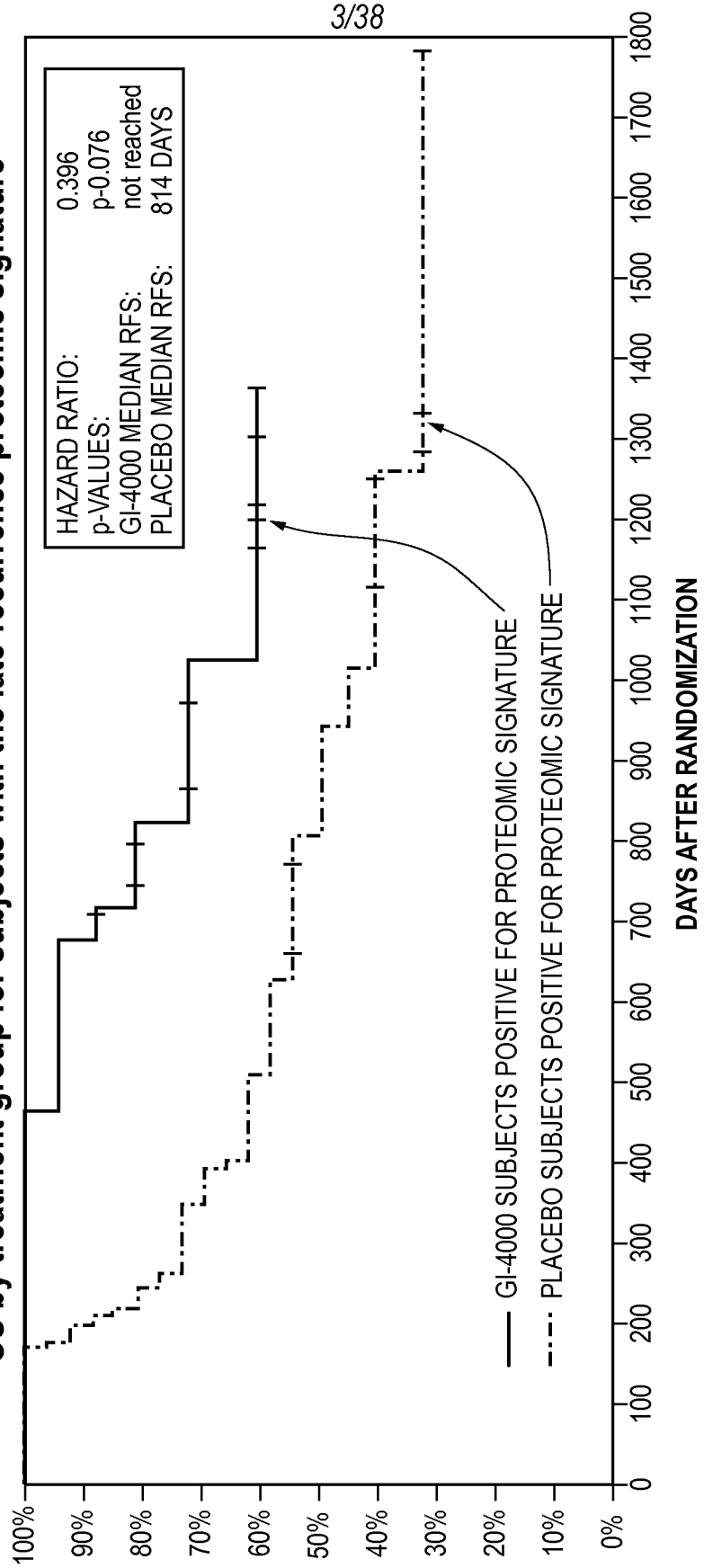

OS by treatment group for subjects with the late-recurrence proteomic signature
HAZARD RATIO: 0.396
p-VALUES: p-0.076
GI-4000 MEDIAN RFS: not reached
PLACEBO MEDIAN RFS: 814 DAYS
GI-4000 SUBJECTS POSITIVE FOR PROTEOMIC SIGNATURE
PLACEBO SUBJECTS POSITIVE FOR PROTEOMIC SIGNATURE
% SUBJECTS RECURRANCE-FREE/ALIVE
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
DAYS AFTER RANDOMIZATION

Fig. 3A

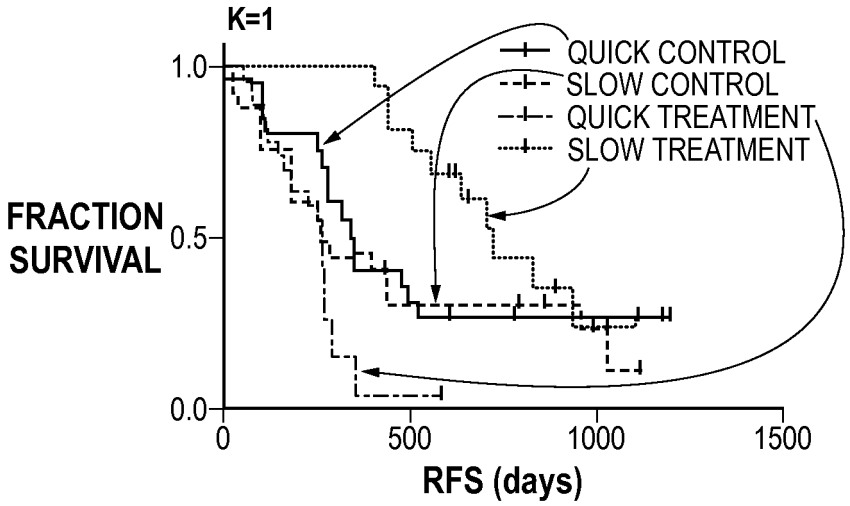

K=1
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 3B

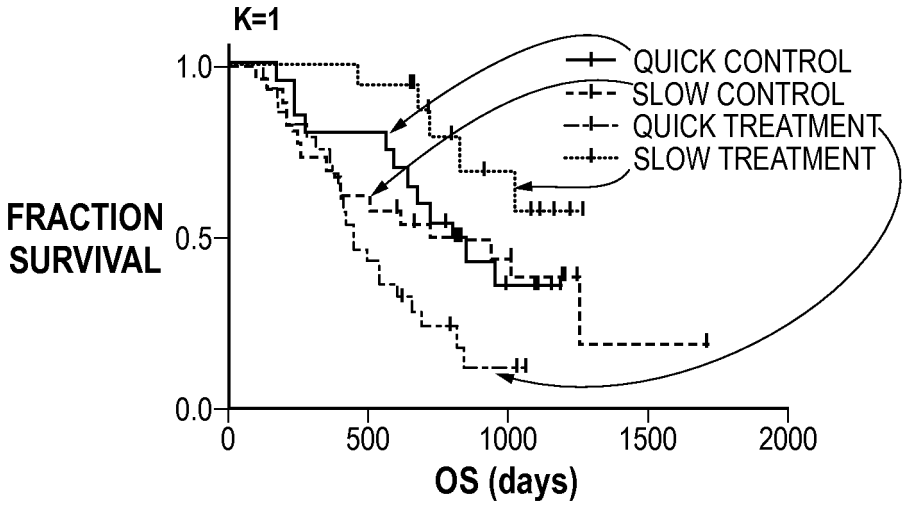

K=1
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 3C

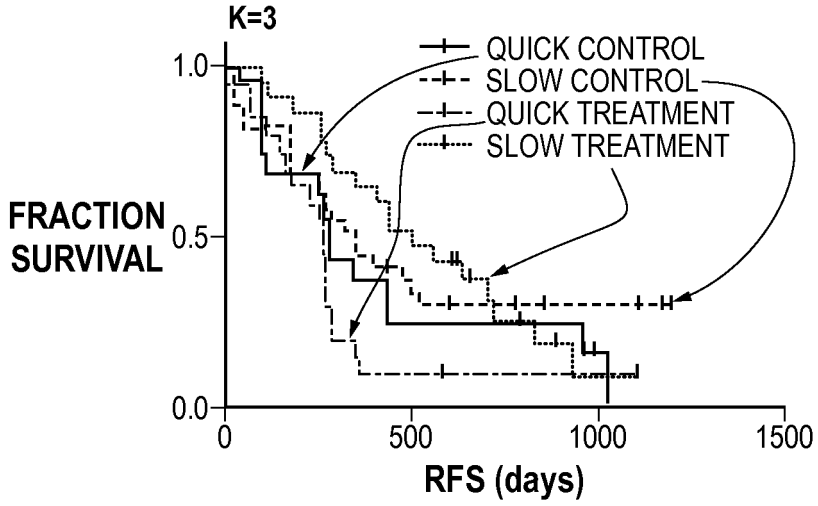

K=3
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 3D

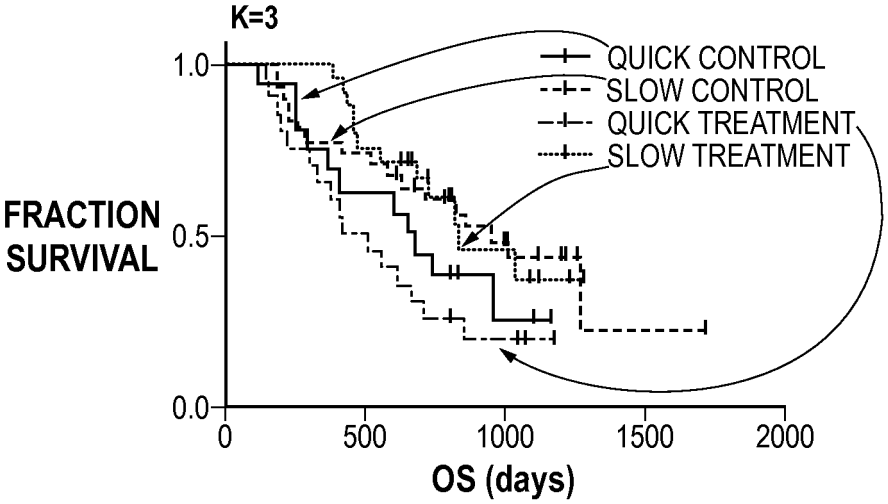

K=3
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 3E

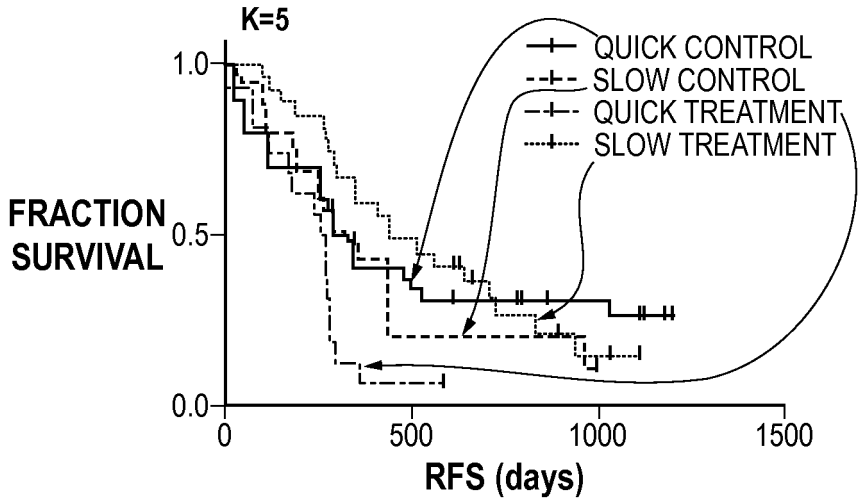

K=5
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 3F

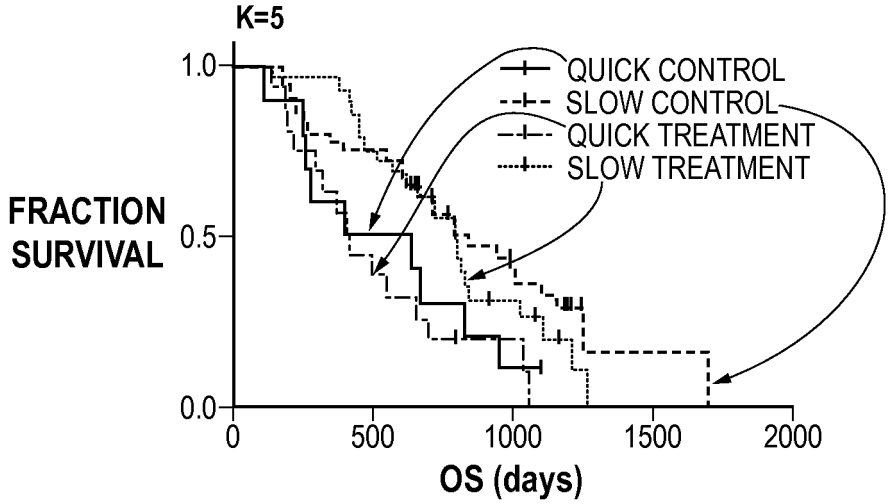

K=5
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 4A

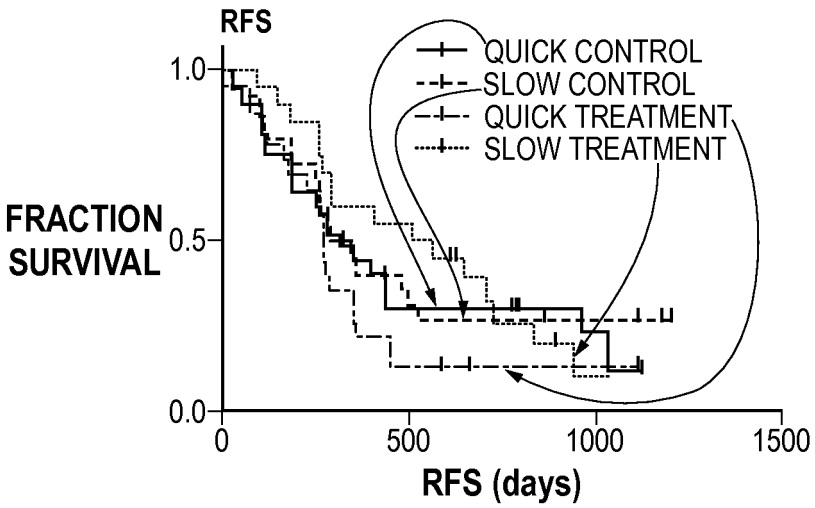

RFS
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 4B

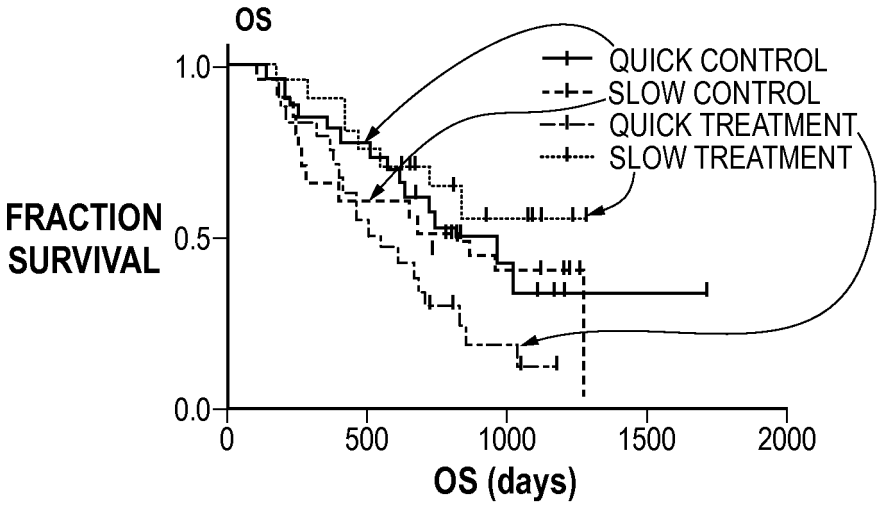

OS
QUICK CONTROL
SLOW CONTROL
QUICK TREATMENT
SLOW TREATMENT
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 4C

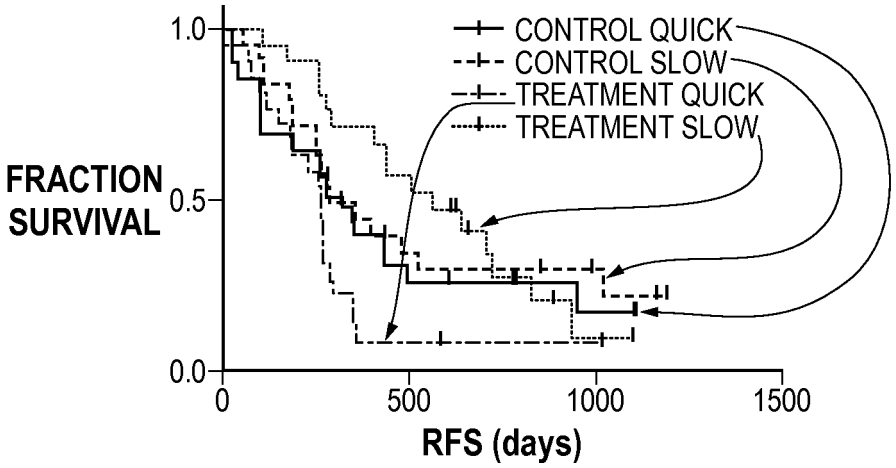

1.0
0.5
0.0
FRACTION SURVIVAL
0
500
1000
1500
RFS (days)
CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW

Fig. 4D

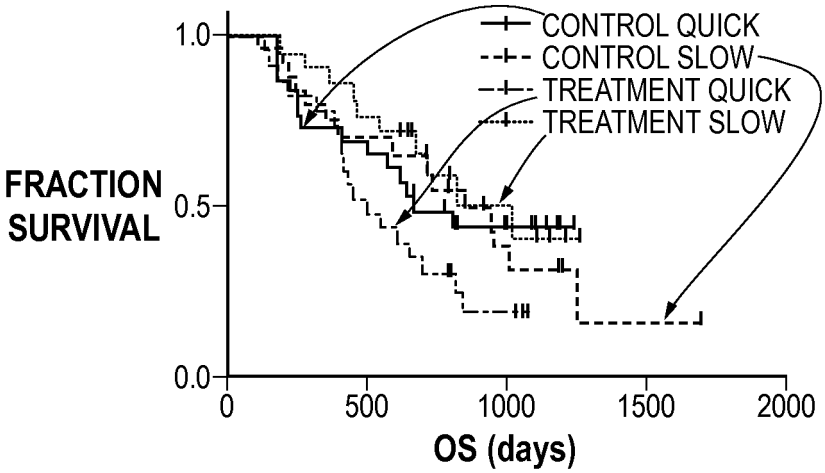

1.0
0.5
0.0
FRACTION SURVIVAL
0
500
1000
1500
2000
OS (days)
CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW

Fig. 4E

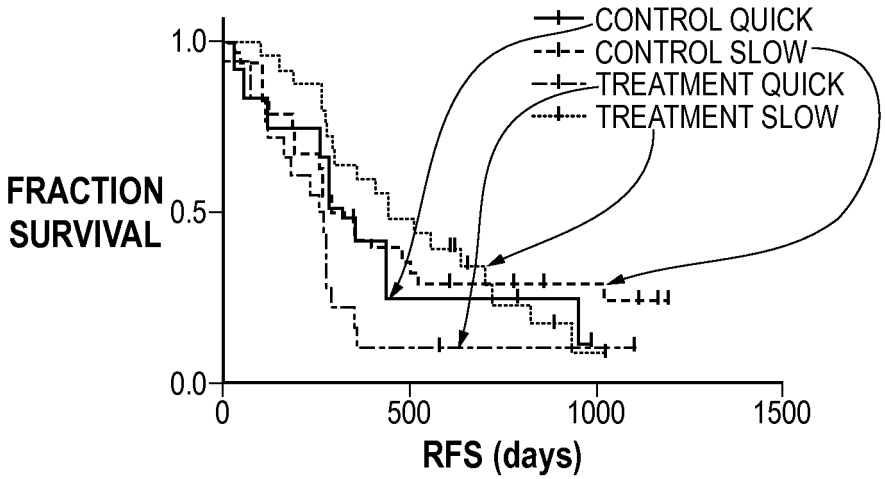

CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 4F

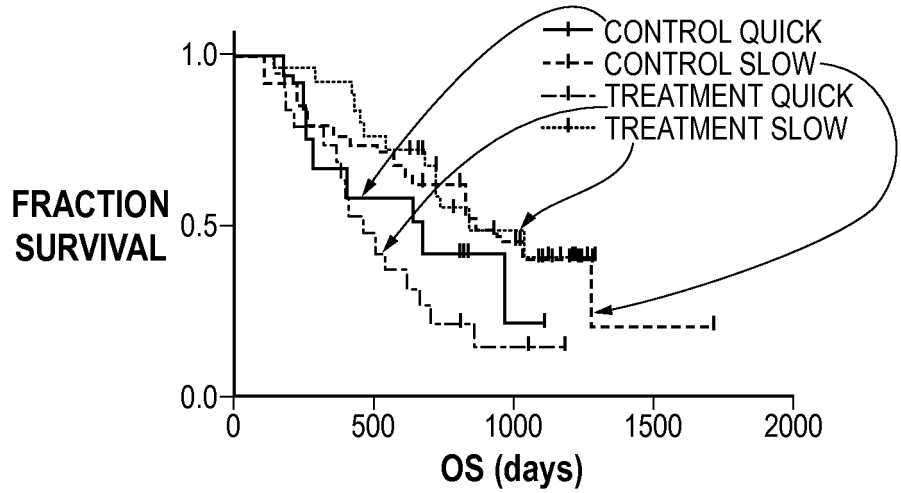

CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 4G

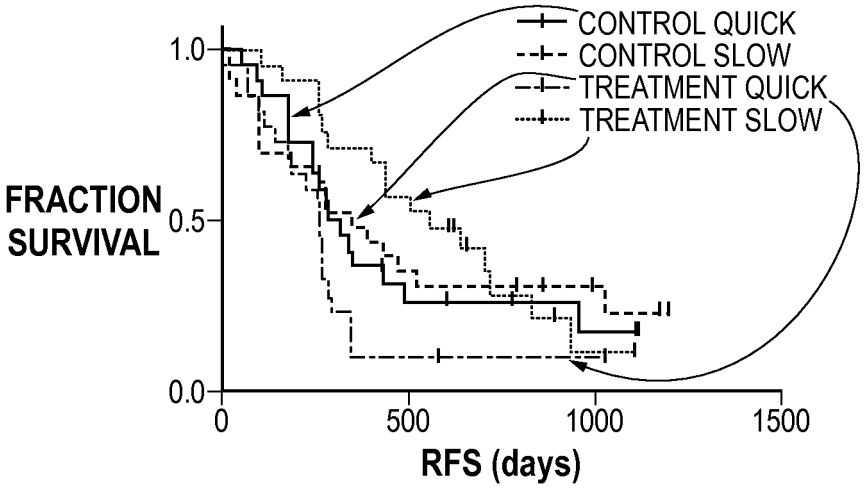

CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
RFS (days)

Fig. 4H

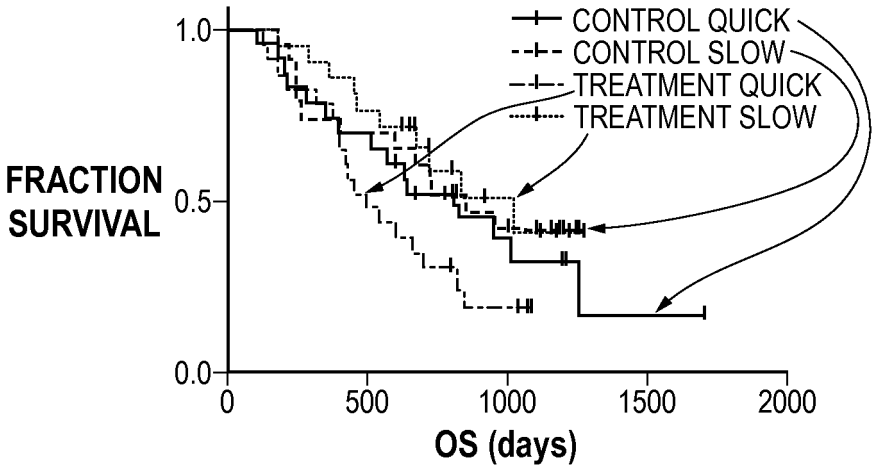

CONTROL QUICK
CONTROL SLOW
TREATMENT QUICK
TREATMENT SLOW
FRACTION SURVIVAL
1.0
0.5
0.0
0
500
1000
1500
2000
OS (days)

Fig. 5

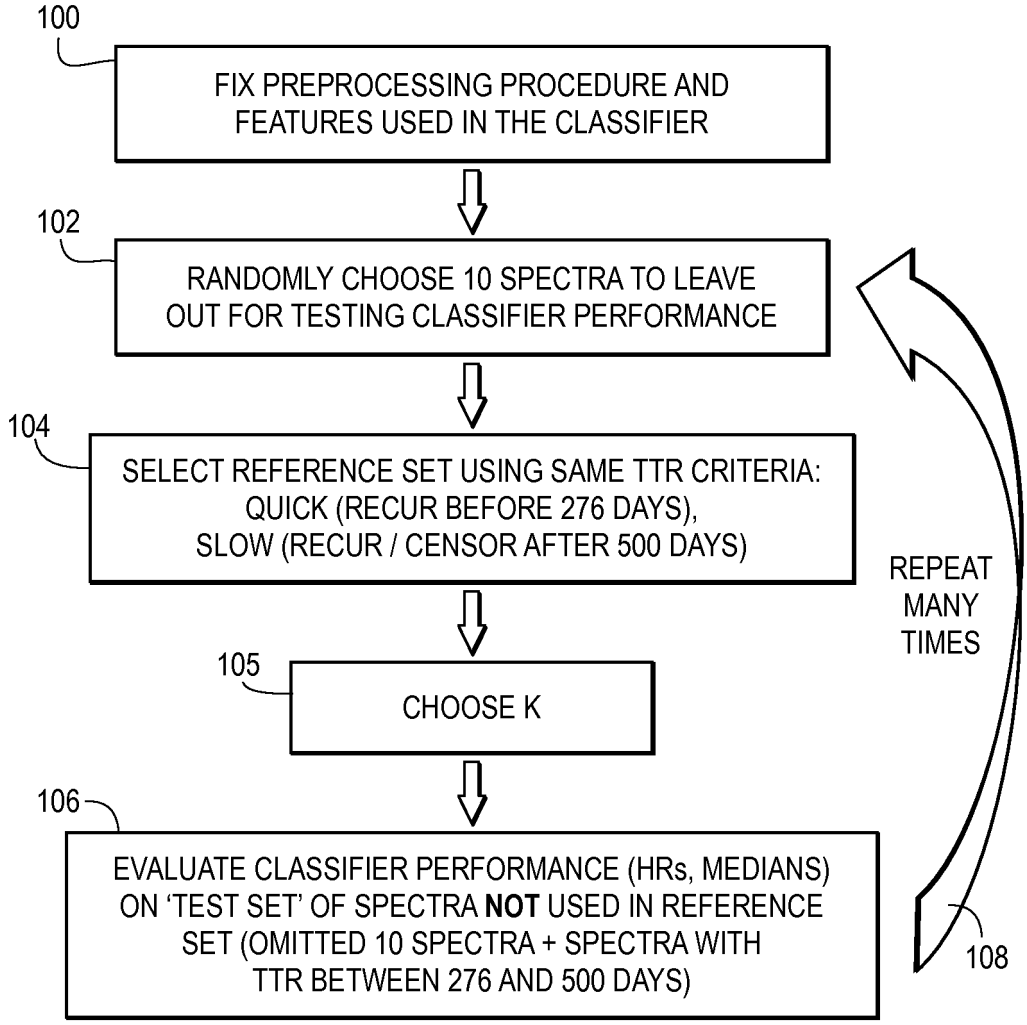

100
FIX PREPROCESSING PROCEDURE AND FEATURES USED IN THE CLASSIFIER
102
RANDOMLY CHOOSE 10 SPECTRA TO LEAVE OUT FOR TESTING CLASSIFIER PERFORMANCE
104
SELECT REFERENCE SET USING SAME TTR CRITERIA: QUICK (RECUR BEFORE 276 DAYS), SLOW (RECUR / CENSOR AFTER 500 DAYS)
105
CHOOSE K
106
EVALUATE CLASSIFIER PERFORMANCE (HRs, MEDIANS) ON 'TEST SET' OF SPECTRA NOT USED IN REFERENCE SET (OMITTED 10 SPECTRA + SPECTRA WITH TTR BETWEEN 276 AND 500 DAYS)
REPEAT MANY TIMES
108

Fig. 6

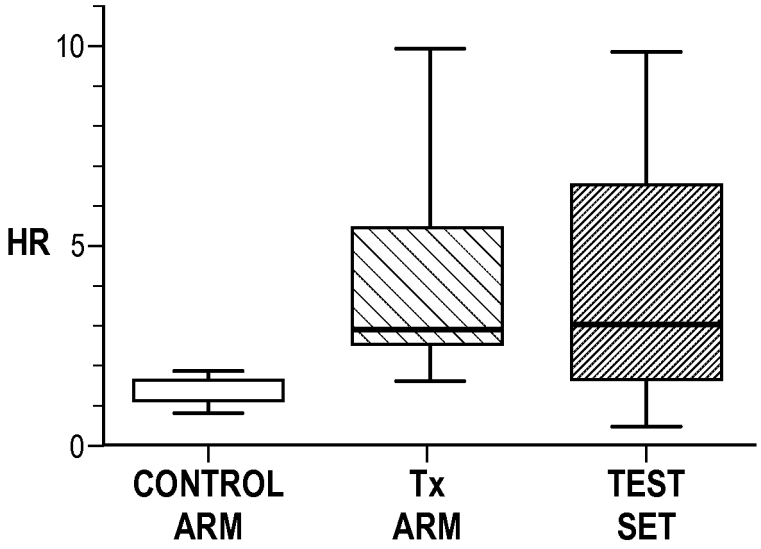

10
HR 5
0
CONTROL ARM
Tx ARM
TEST SET

Fig. 7A

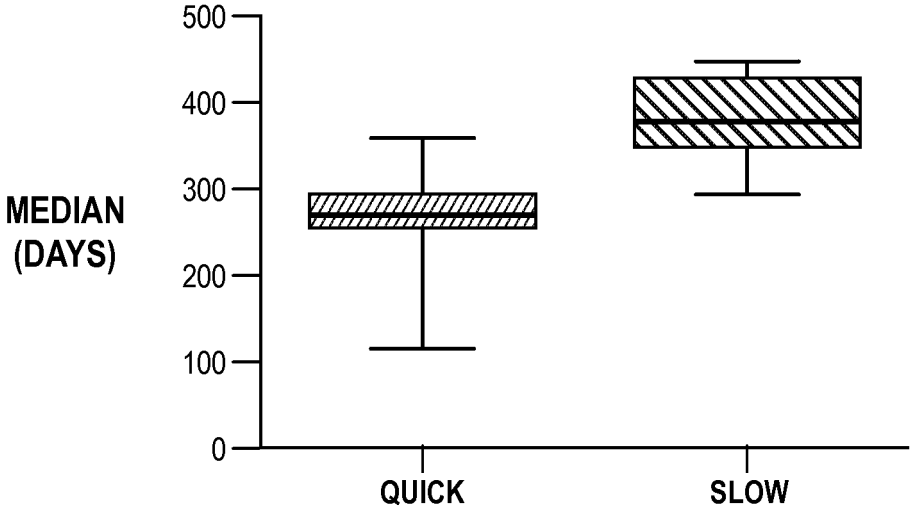

500
400
300
200
100
0
MEDIAN (DAYS)
QUICK
SLOW

Fig. 7B

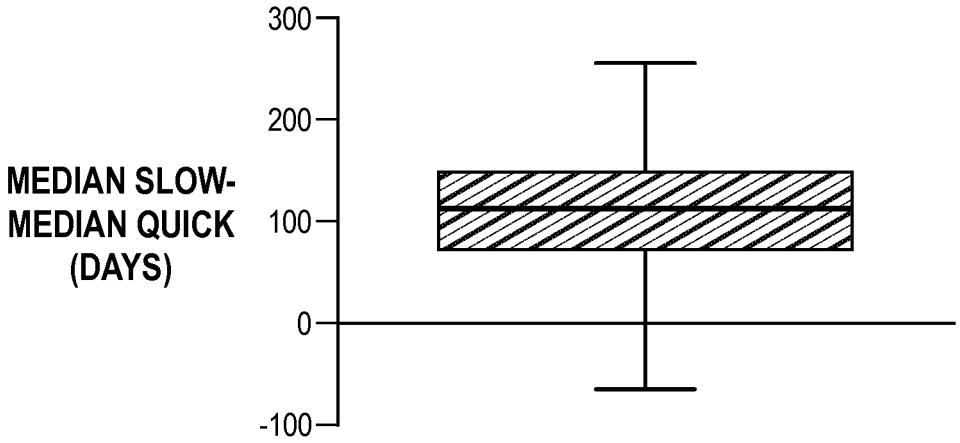

300
200
100
0
-100
MEDIAN SLOW-
MEDIAN QUICK
(DAYS)

Fig. 8

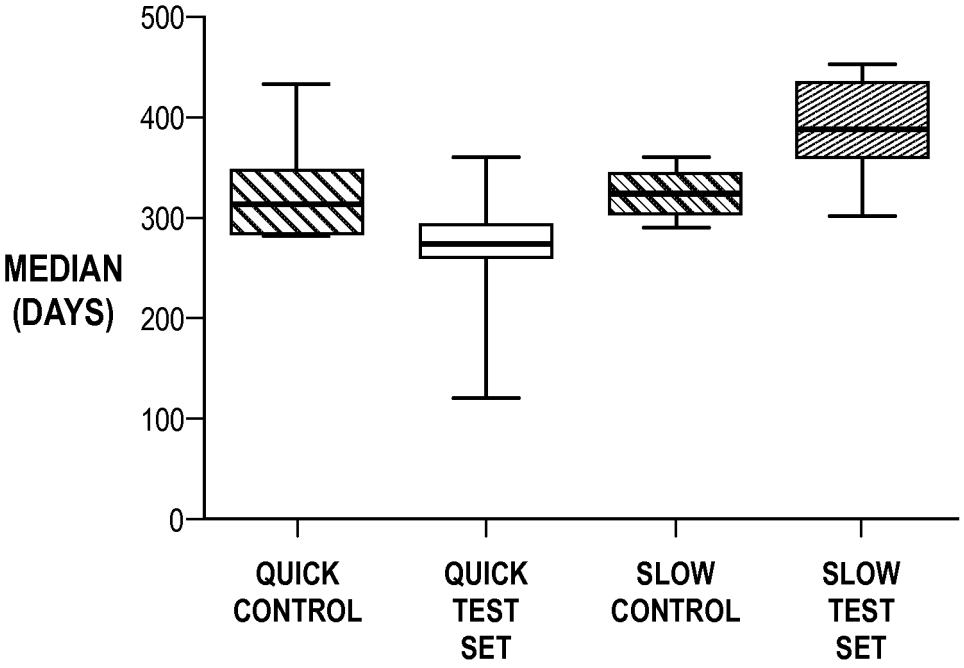

500
400
300
200
100
0
MEDIAN
(DAYS)
QUICK
CONTROL
QUICK
TEST
SET
SLOW
CONTROL
SLOW
TEST
SET

Fig. 9

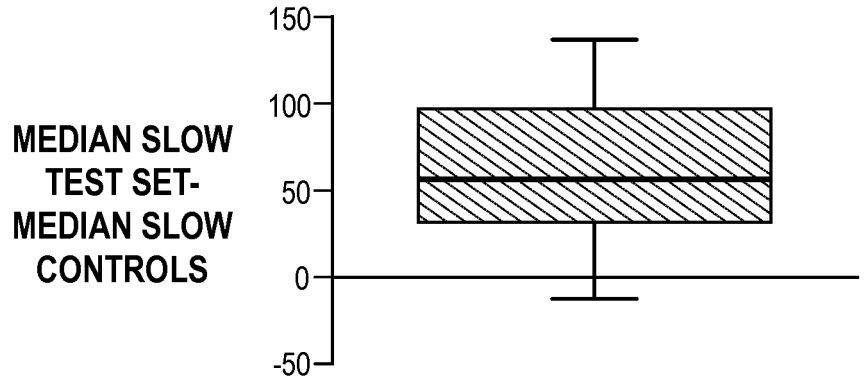

MEDIAN SLOW TEST SET- MEDIAN SLOW CONTROLS
150
100
50
0
-50

Fig. 10A

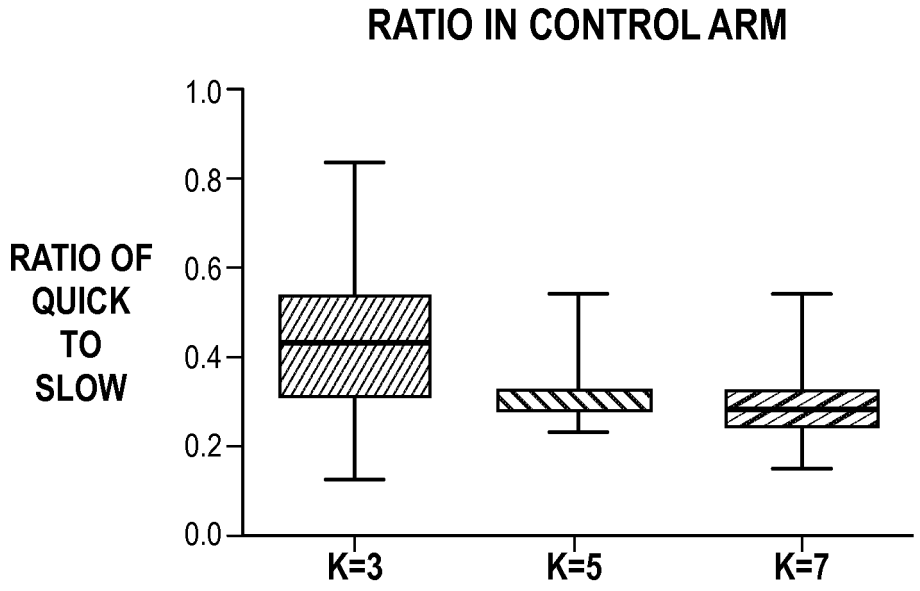
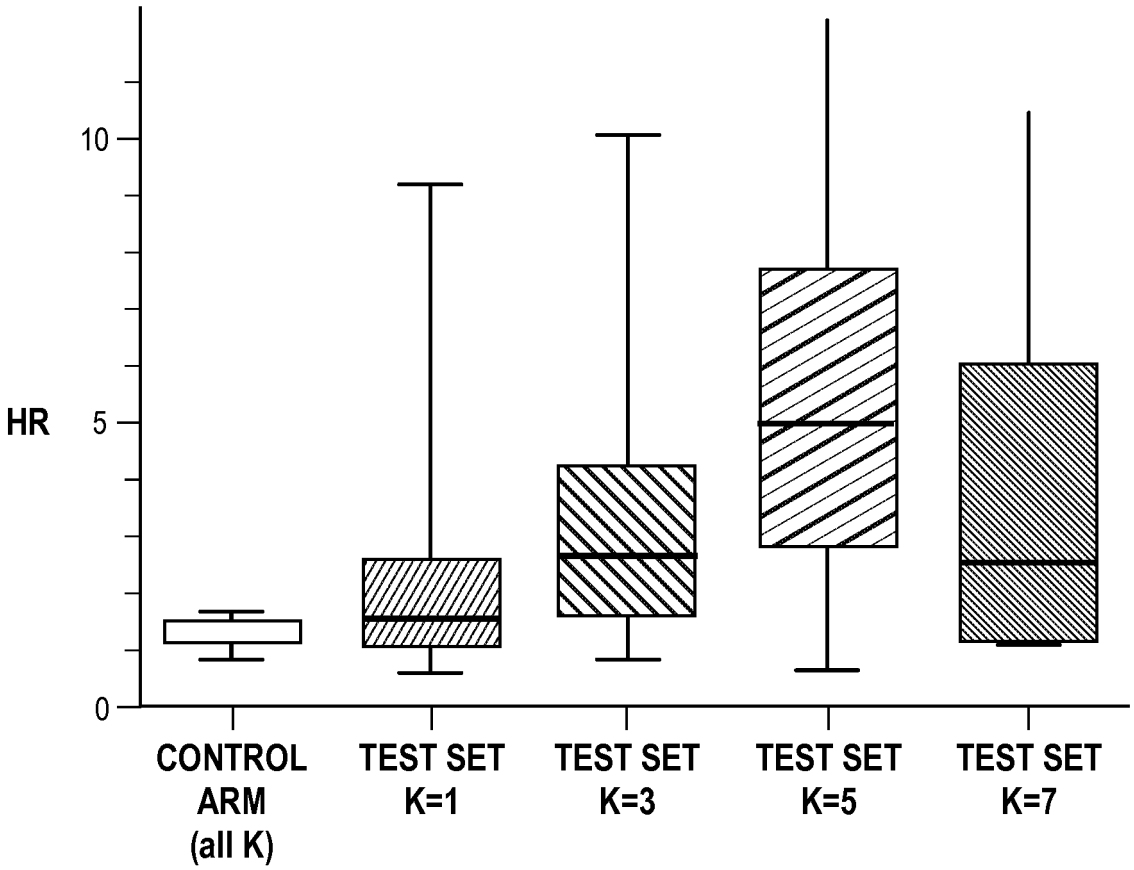

RATIO IN CONTROL ARM
RATIO OF QUICK TO SLOW
1.0
0.8
0.6
0.4
0.2
0.0
K=3
K=5
K=7

Fig. 10B



HAZARD RATIOS FOR TEST SET OF CROSS-VALIDATION ANALYSES, VARIOUS K VALUES

Fig. 11

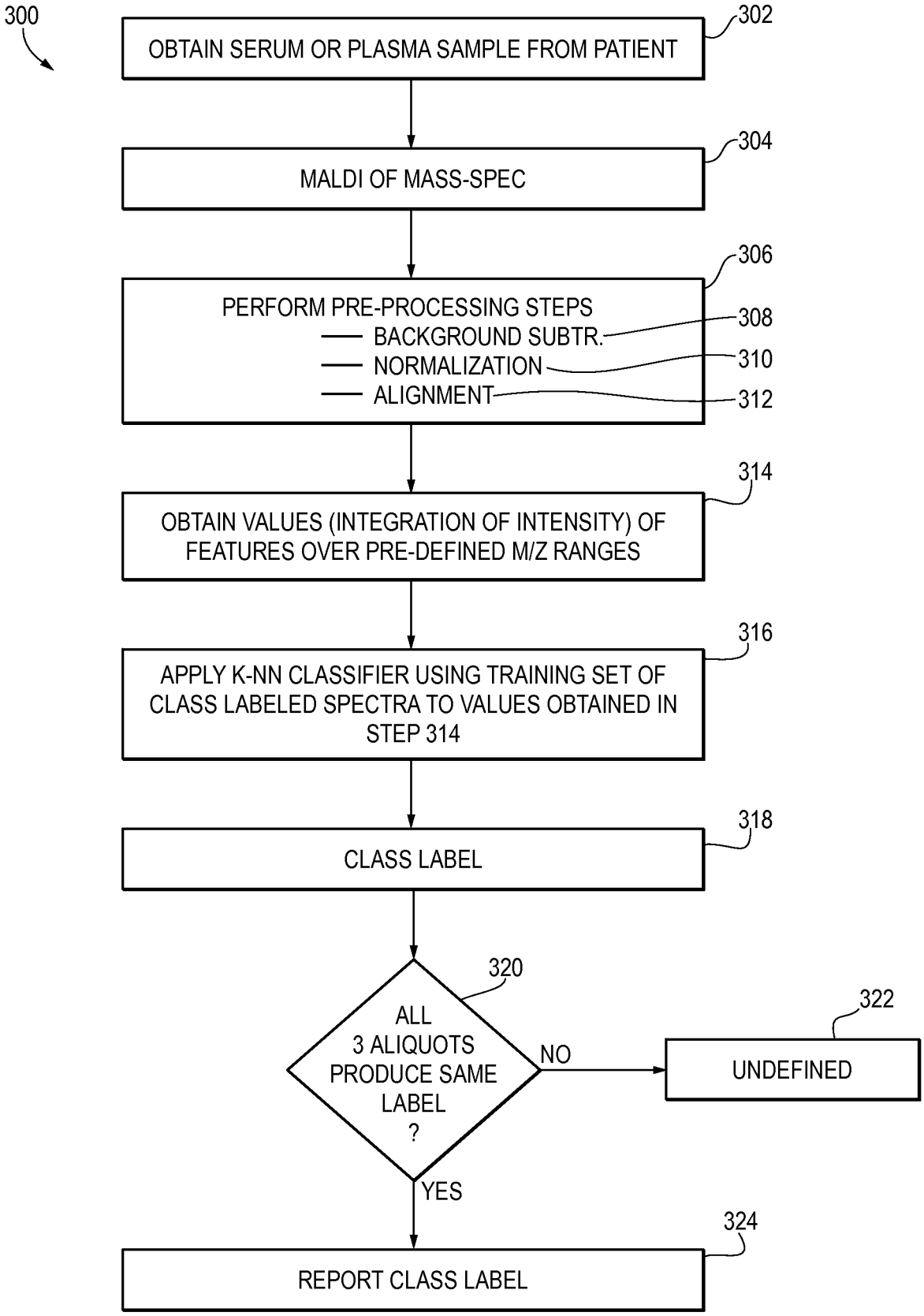

300
OBTAIN SERUM OR PLASMA SAMPLE FROM PATIENT
302
MALDI OF MASS-SPEC
304
PERFORM PRE-PROCESSING STEPS
BACKGROUND SUBTR.
NORMALIZATION
ALIGNMENT
306
308
310
312
OBTAIN VALUES (INTEGRATION OF INTENSITY) OF FEATURES OVER PRE-DEFINED M/Z RANGES
314
APPLY K-NN CLASSIFIER USING TRAINING SET OF CLASS LABELED SPECTRA TO VALUES OBTAINED IN STEP 314
316
CLASS LABEL
318
ALL 3 ALIQUOTS PRODUCE SAME LABEL ?
320
NO
UNDEFINED
322
YES
REPORT CLASS LABEL
324

Fig. 12

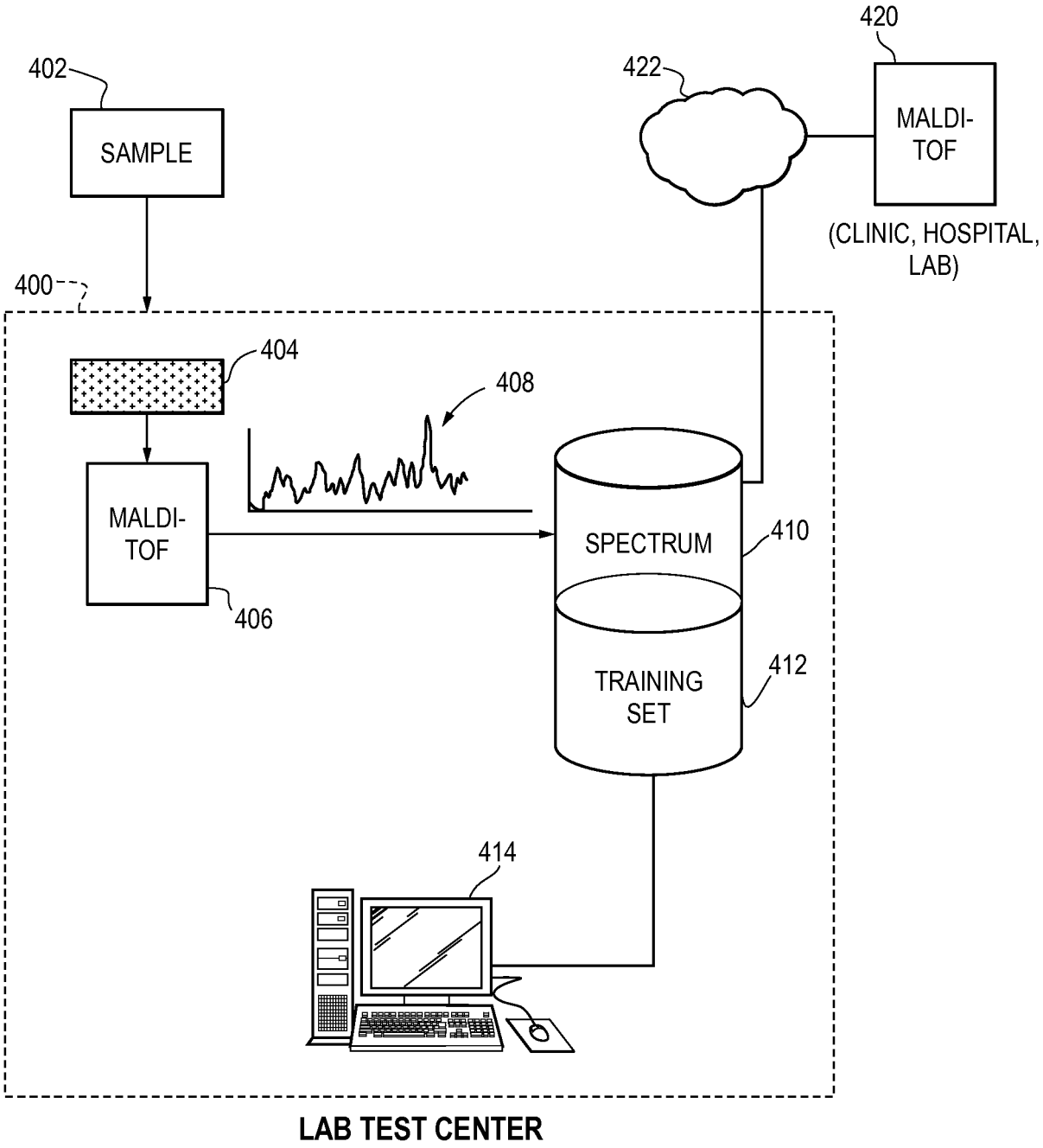

420
402
422
SAMPLE
MALDI-
TOF
(CLINIC, HOSPITAL,
LAB)
400
404
408
MALDI-
TOF
SPECTRUM
410
406
TRAINING
SET
412
414
LAB TEST CENTER

Fig. 13A

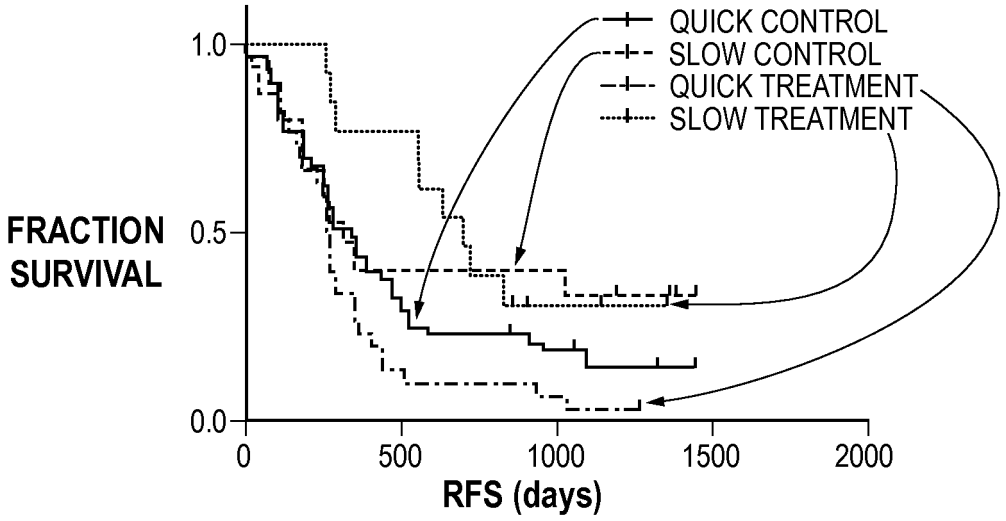


Fig. 13B

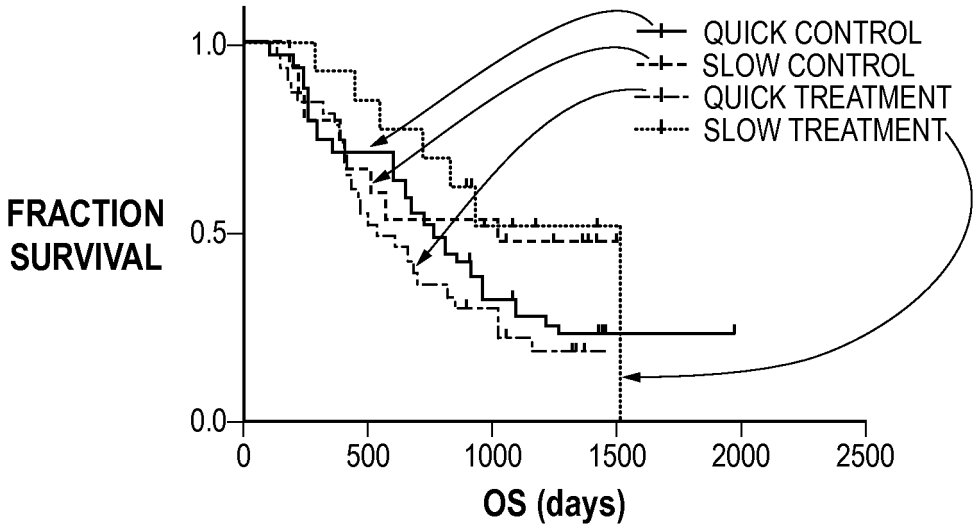


Fig. 13C

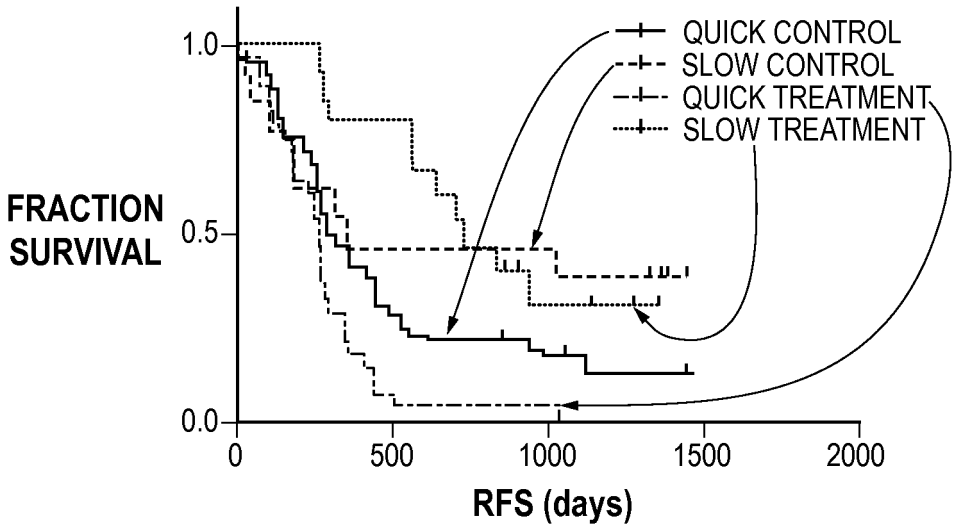


Fig. 13D

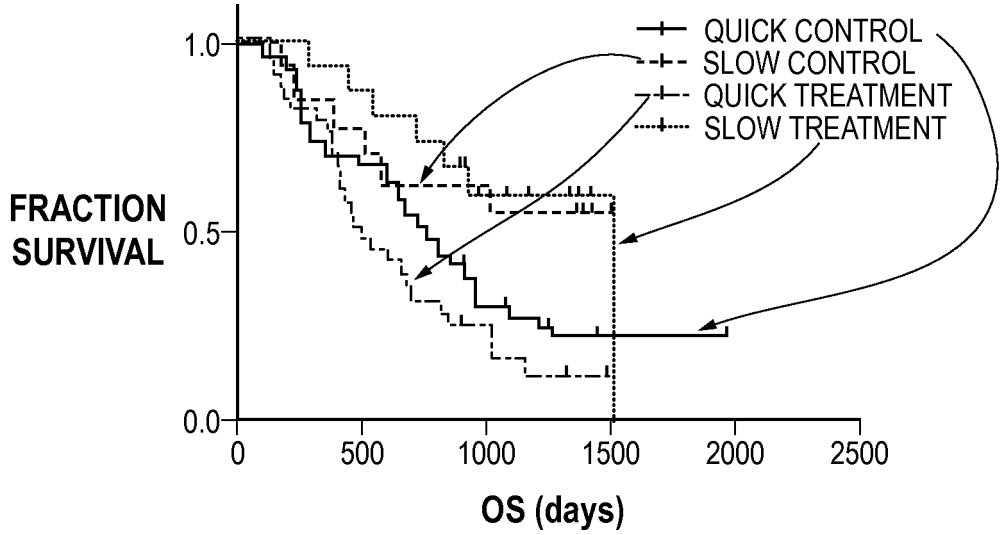


Fig. 13E

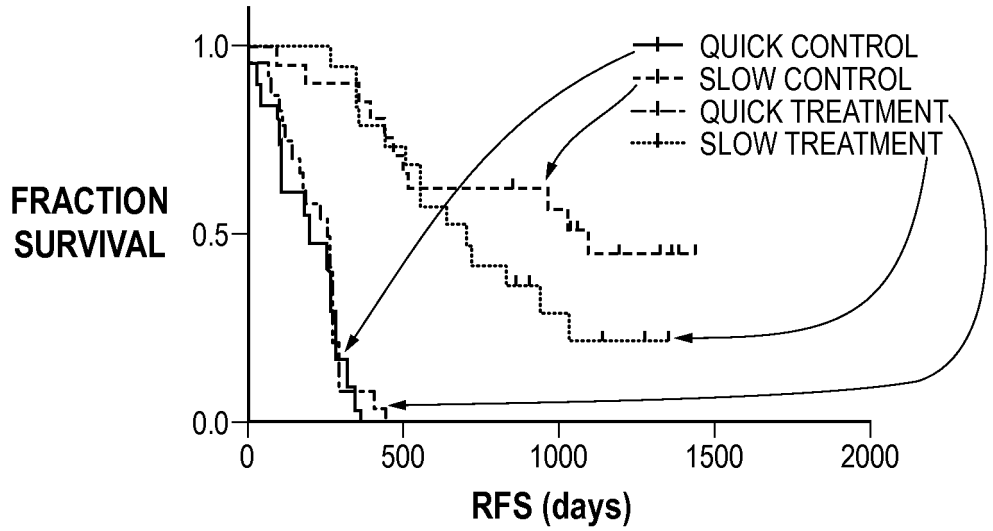


Fig. 13F

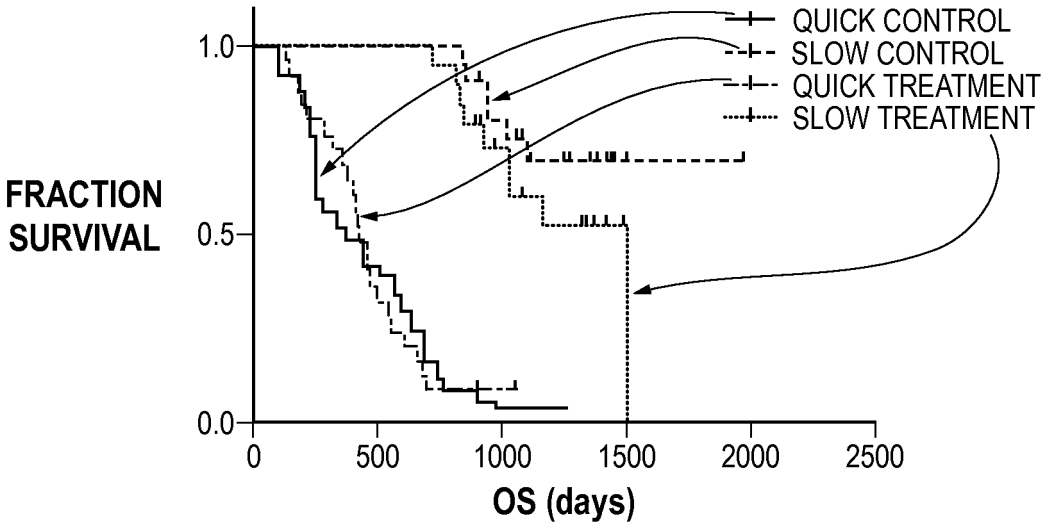


Fig. 13G

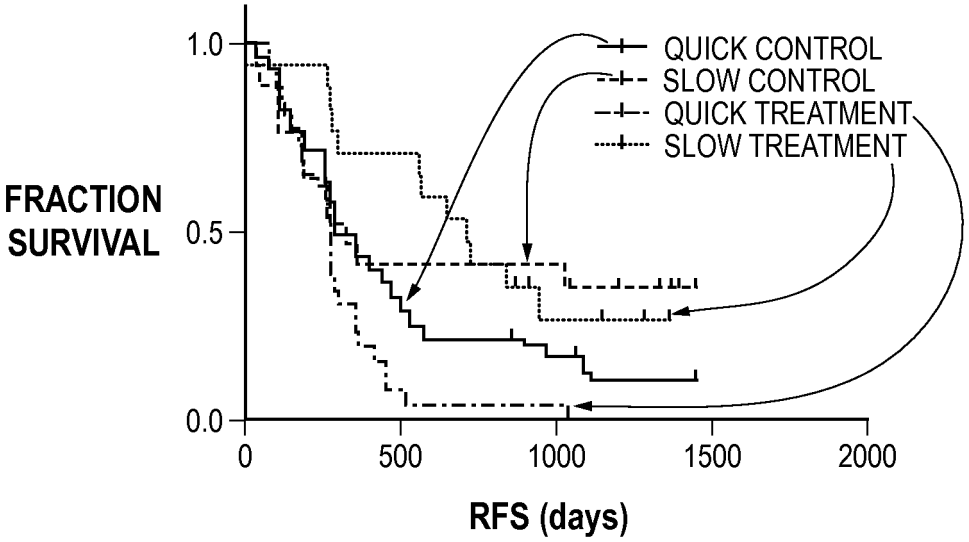


Fig. 13H

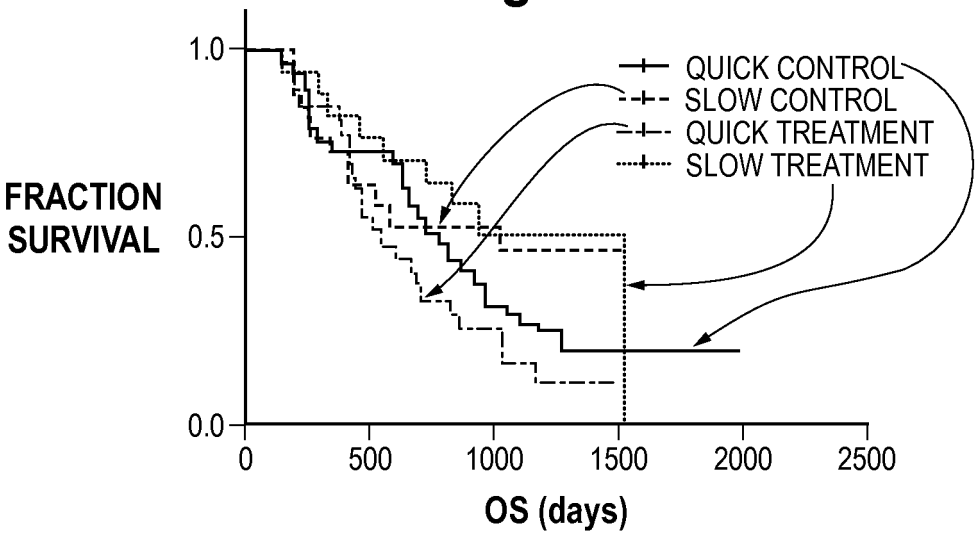


Fig. 13I

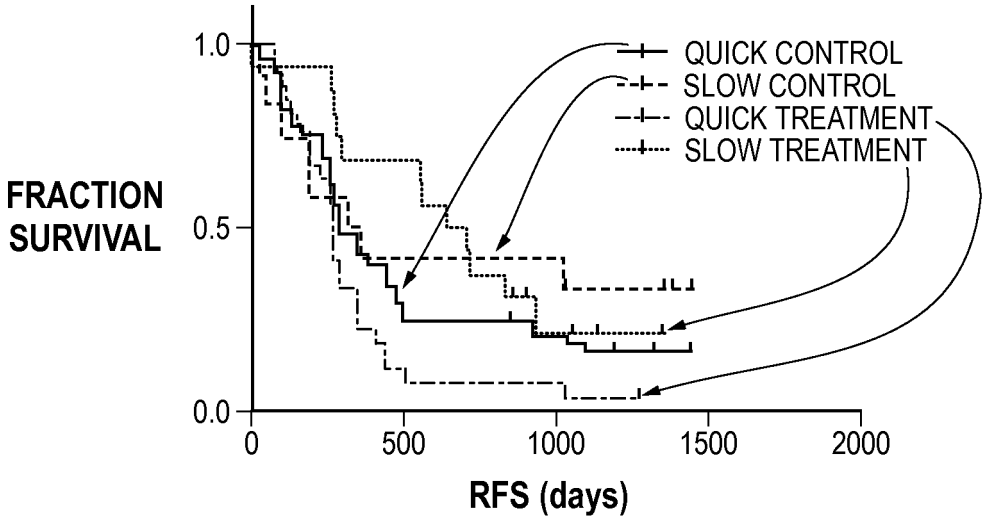


Fig. 13J

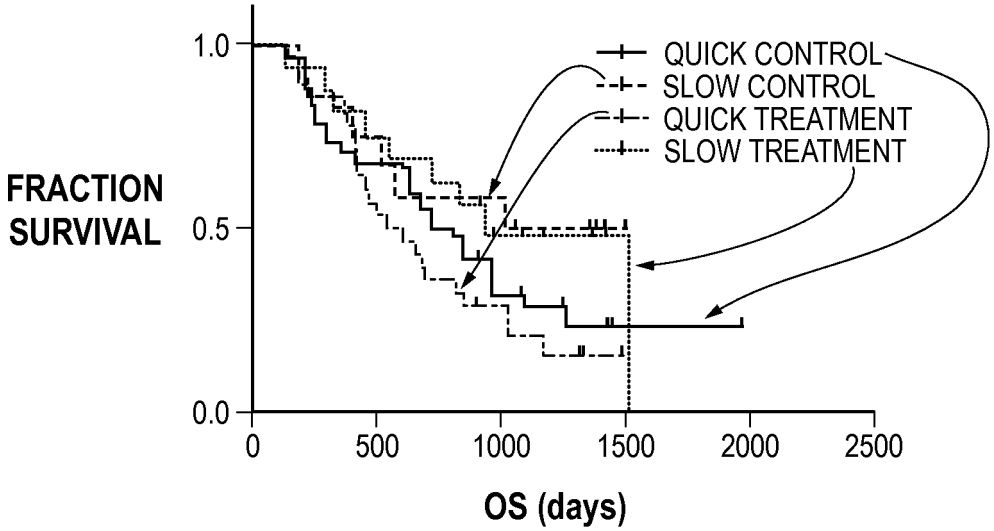


Fig. 13K

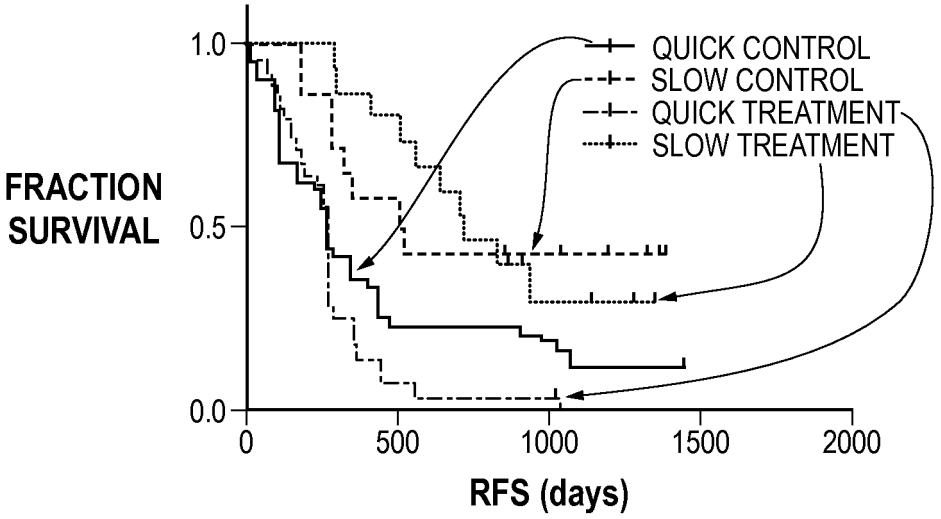


Fig. 13L

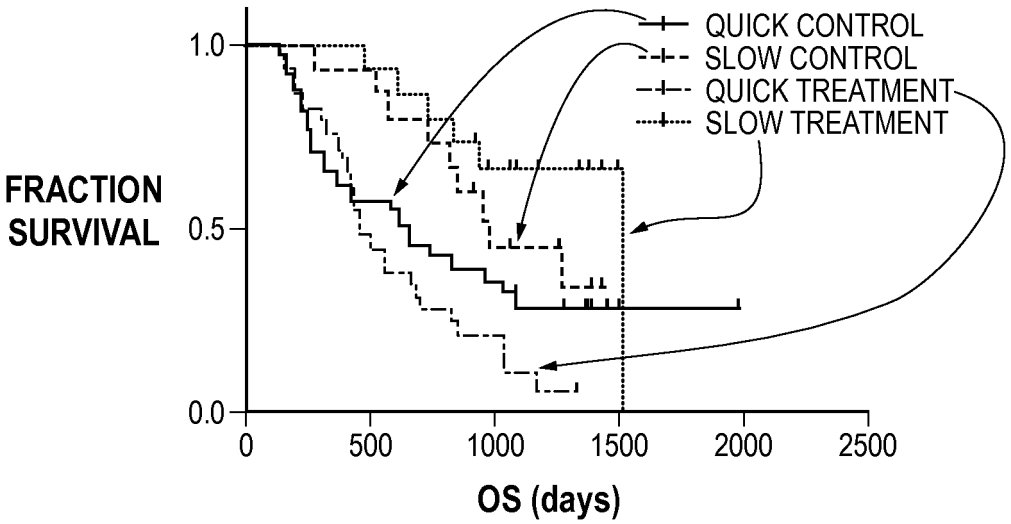


Fig. 14

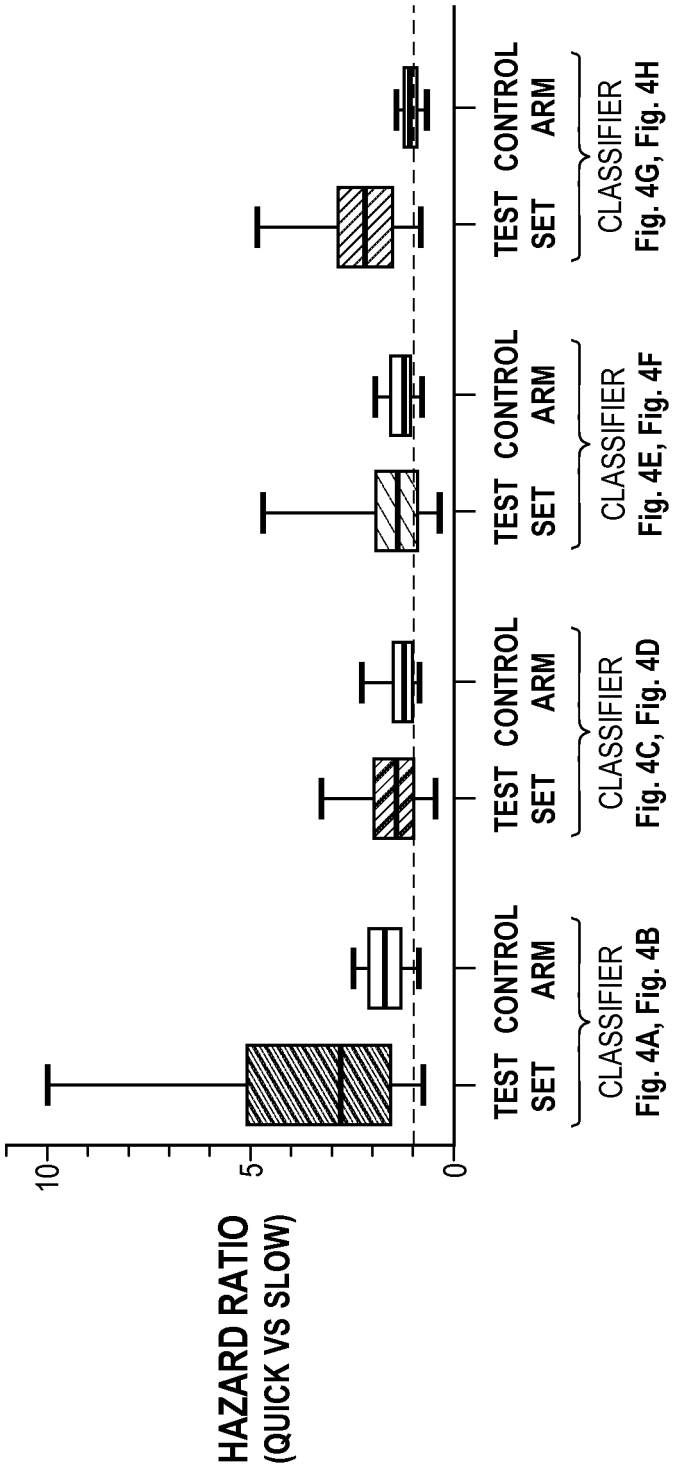

HAZARD RATIO
(QUICK VS SLOW)
10
5
0
TEST SET
CONTROL ARM
CLASSIFIER
Fig. 4A, Fig. 4B
TEST SET
CONTROL ARM
CLASSIFIER
Fig. 4C, Fig. 4D
TEST SET
CONTROL ARM
CLASSIFIER
Fig. 4E, Fig. 4F
TEST SET
CONTROL ARM
CLASSIFIER
Fig. 4G, Fig. 4H

Fig. 15

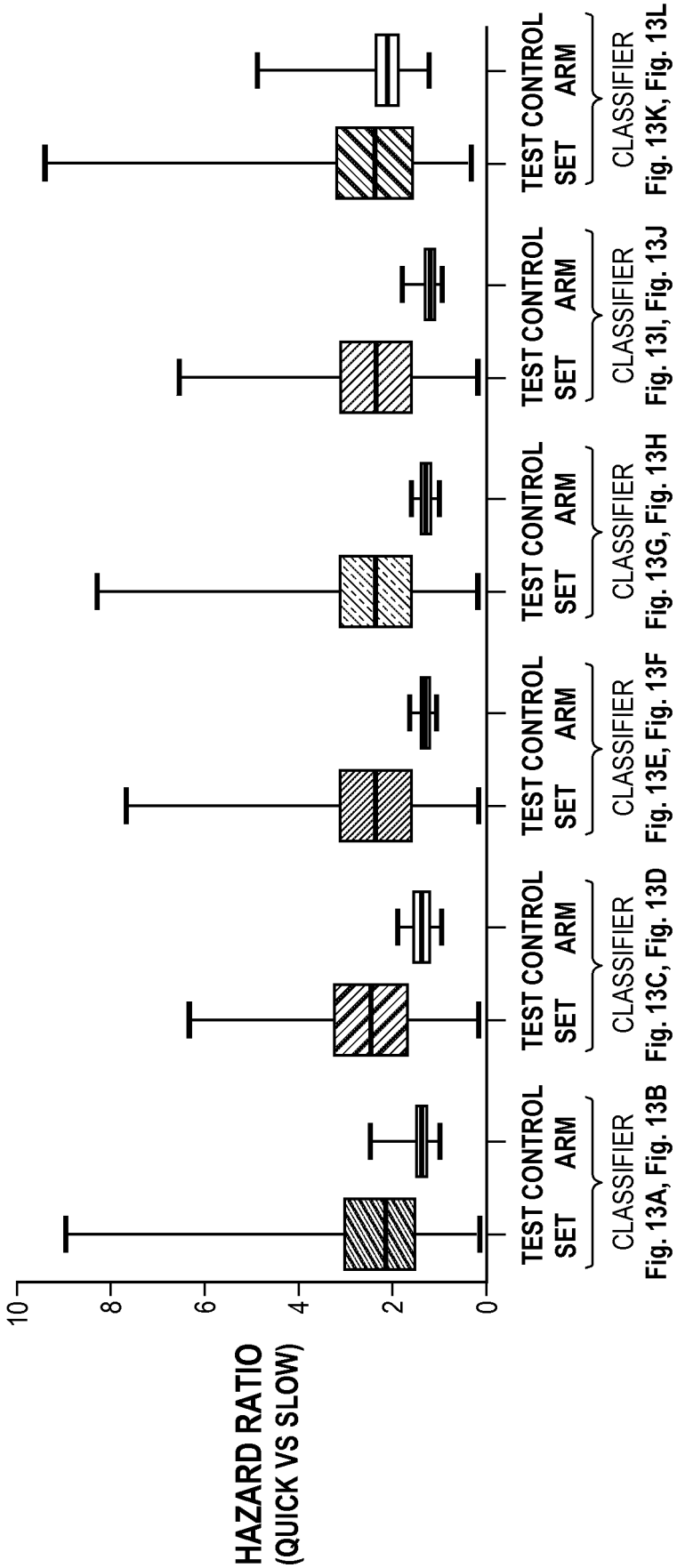

HAZARD RATIO
(QUICK VS SLOW)
10
8
6
4
2
0
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13A, Fig. 13B
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13C, Fig. 13D
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13E, Fig. 13F
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13G, Fig. 13H
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13I, Fig. 13J
TEST CONTROL
SET ARM
CLASSIFIER
Fig. 13K, Fig. 13L

Fig. 16A

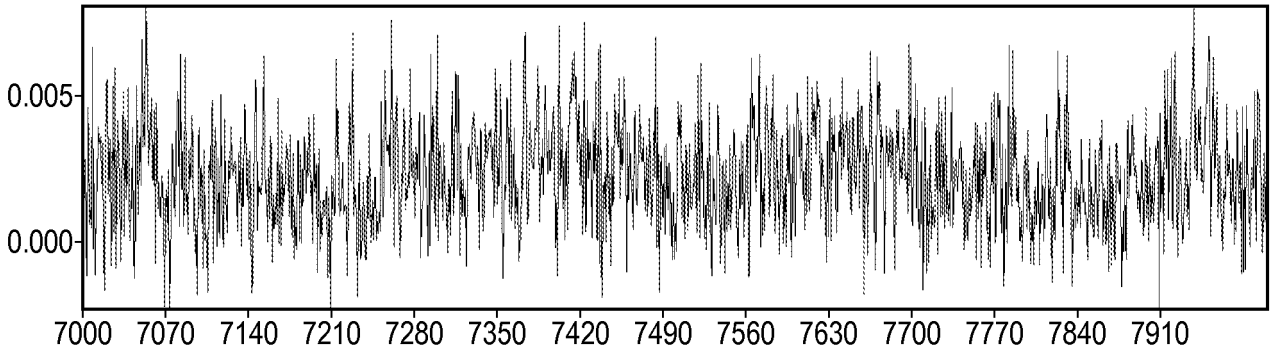


Fig. 16B

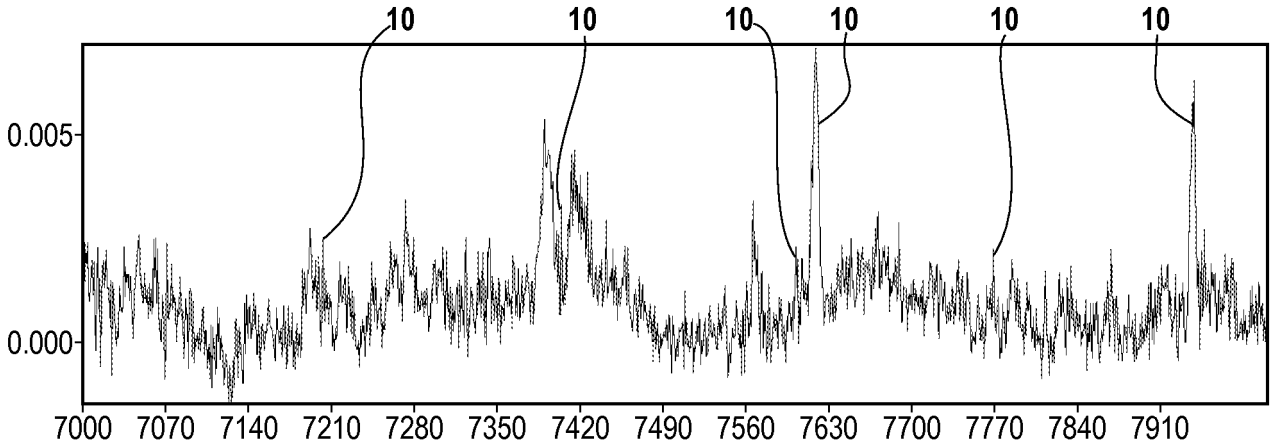
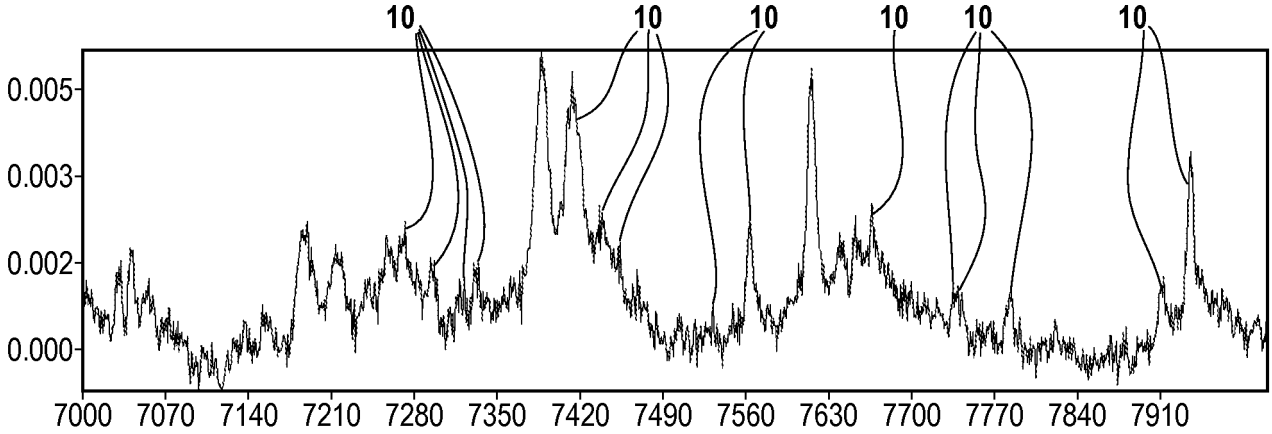


Fig. 16C



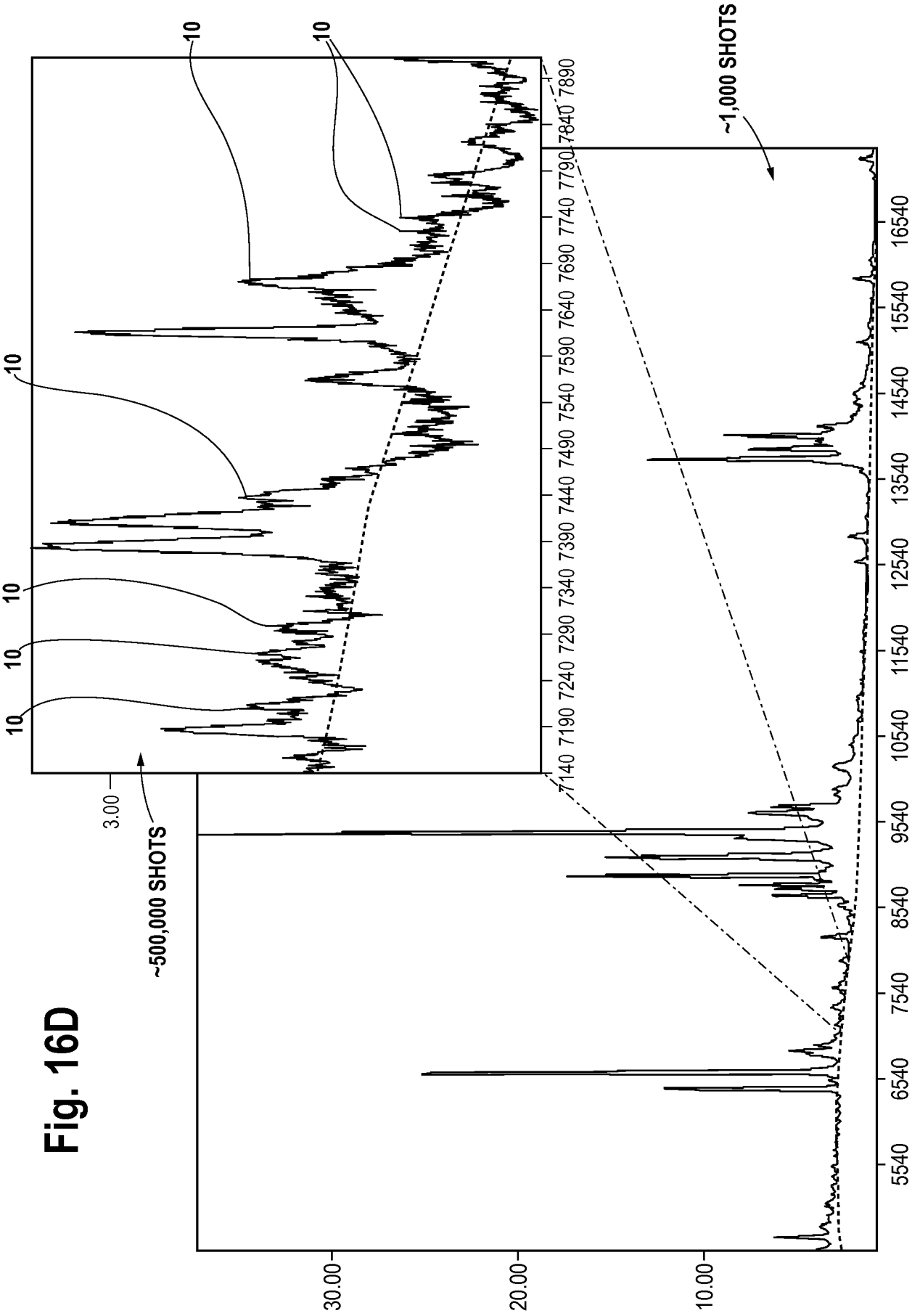

~500,000 SHOTS
~1,000 SHOTS
3.00
30.00
20.00
10.00
10
5540
6540
7540
8540
9540
10540
11540
12540
13540
14540
15540
16540
7140
7190
7240
7290
7340
7390
7440
7490
7540
7590
7640
7690
7740
7790
7840
7890

Fig. 16D

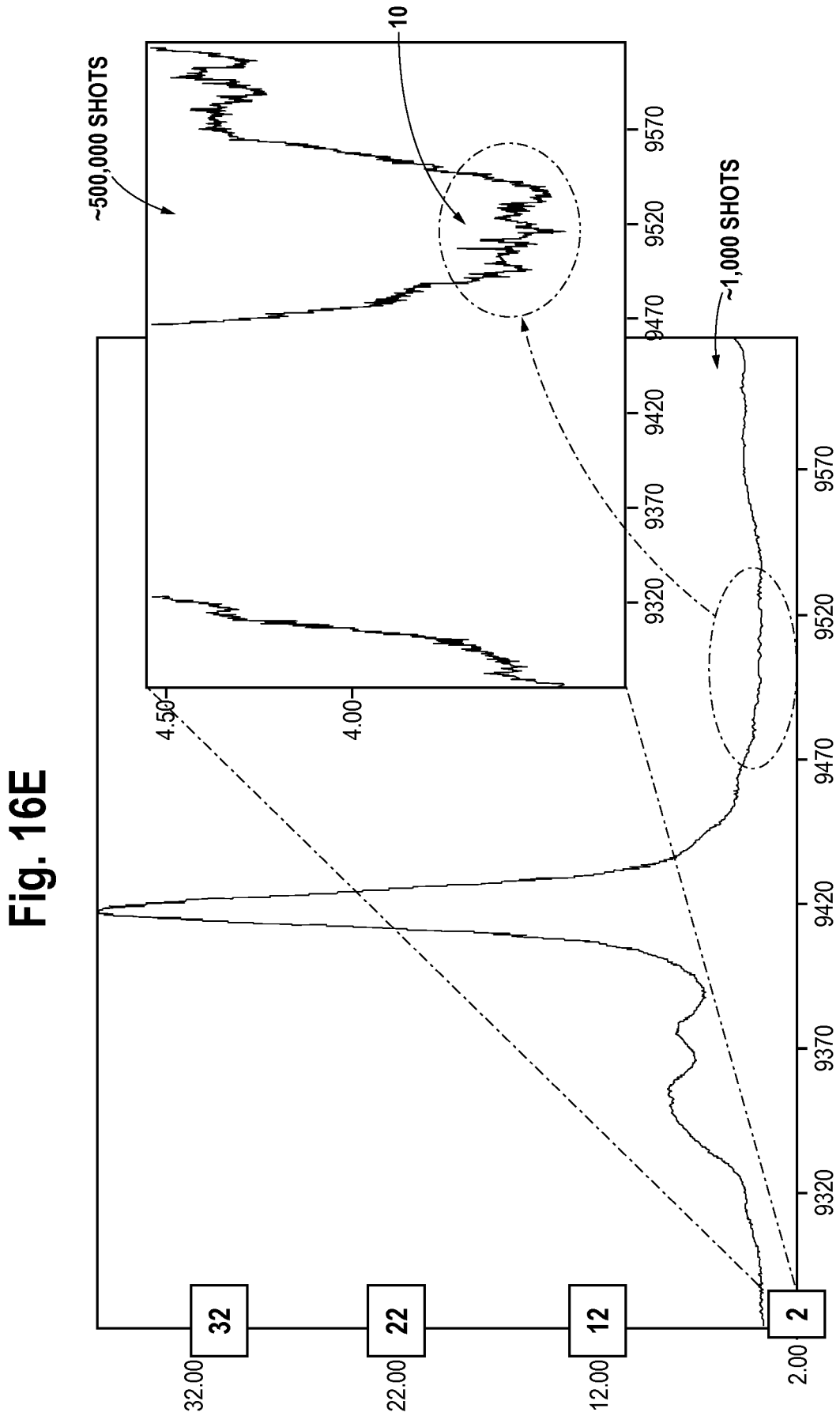

~500,000 SHOTS
10
~1,000 SHOTS
4.50
4.00
9320
9370
9420
9470
9520
9570
32
22
12
2
32.00
22.00
12.00
2.00

Fig. 16E

Fig. 17A

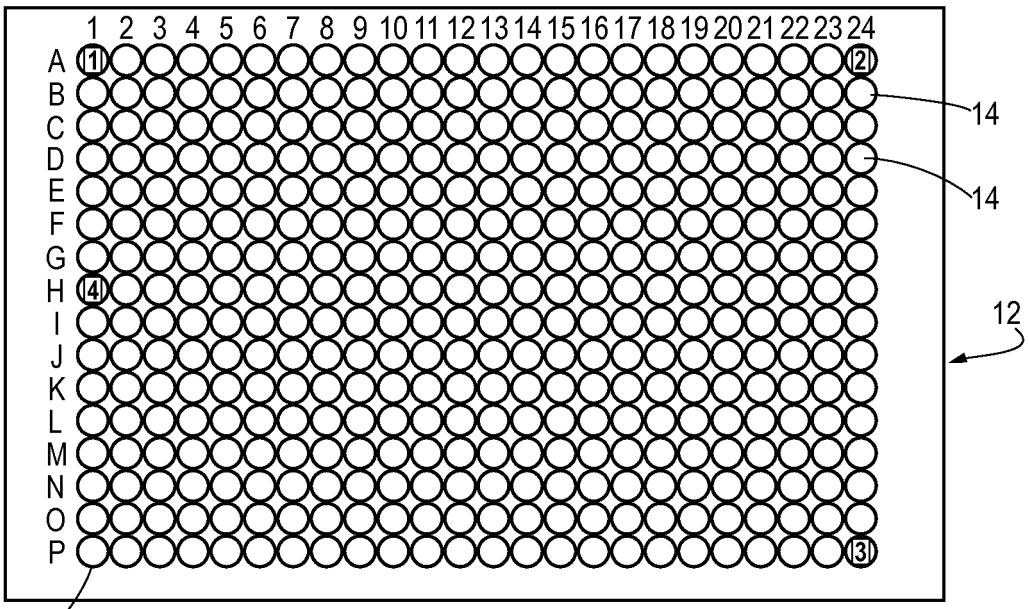
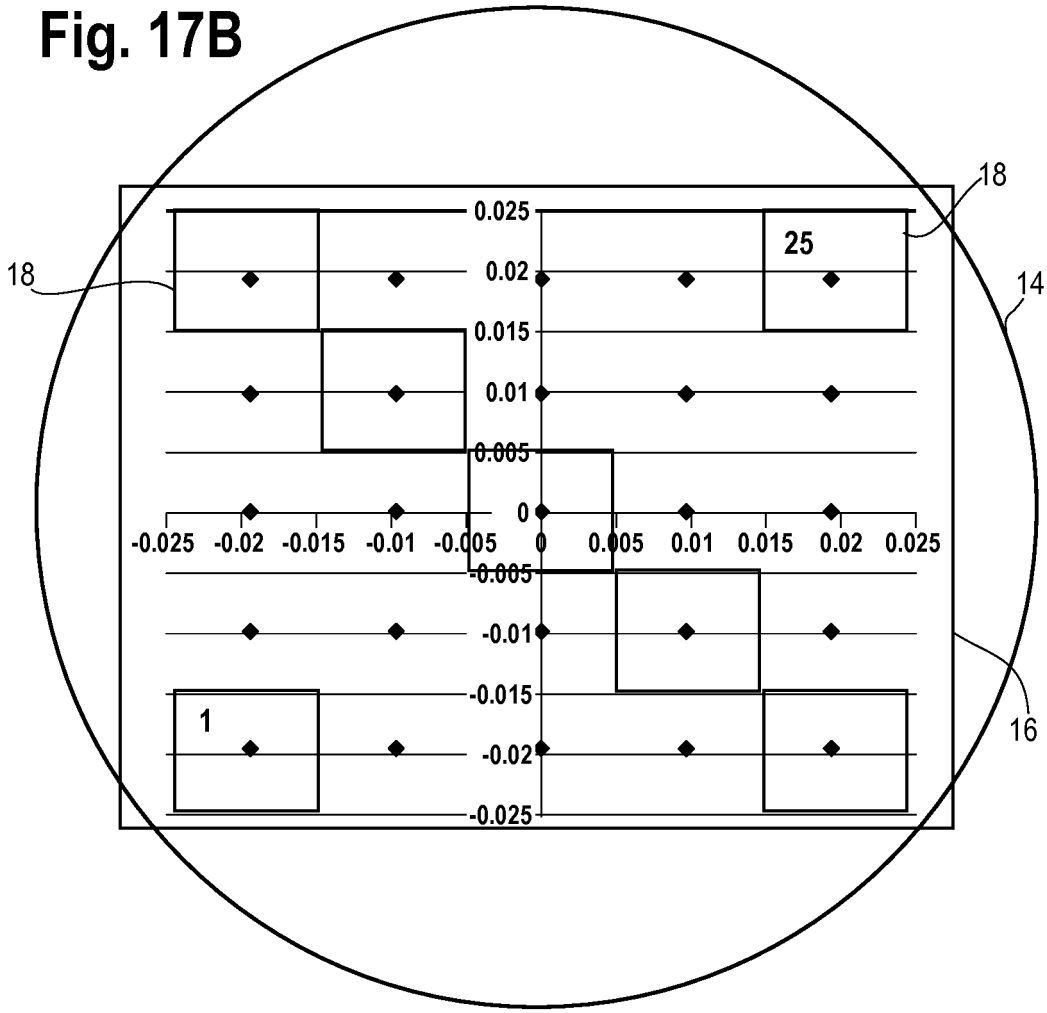


Fig. 14B

Fig. 17B



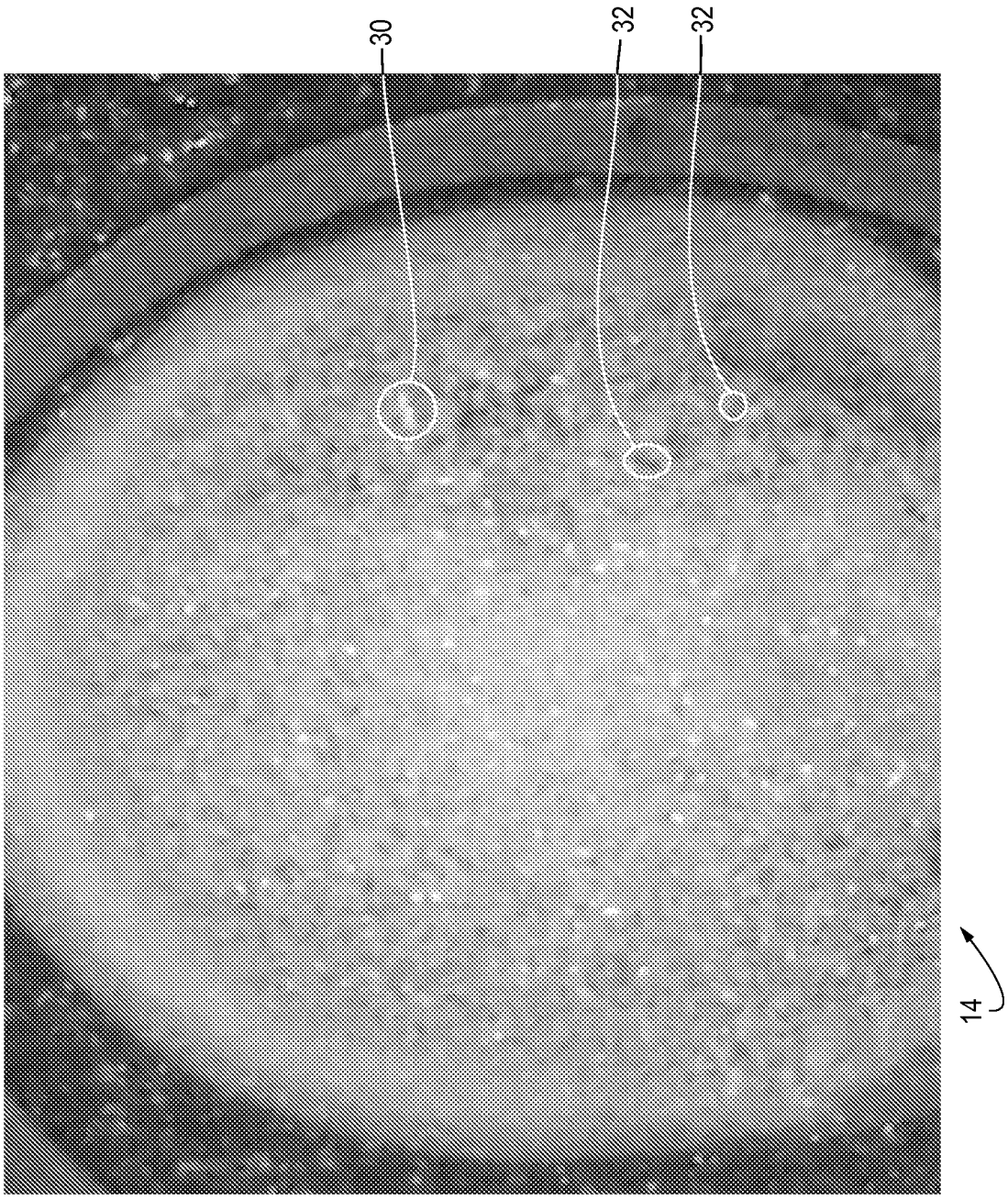


Fig. 18

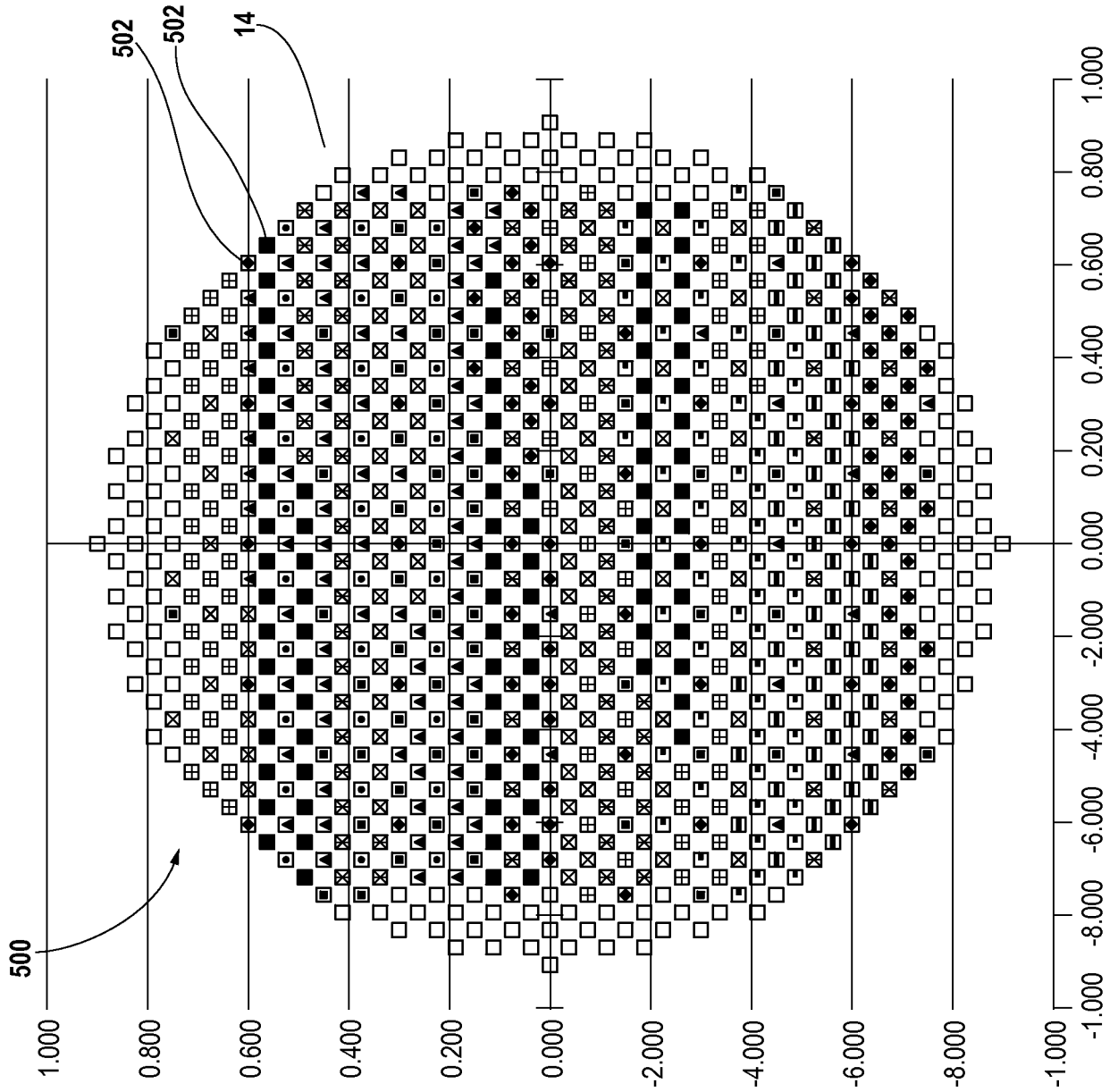

502
502
14
500
1.000
0.800
0.600
0.400
0.200
0.000
-2.000
-4.000
-6.000
-8.000
-1.000
1.000
0.800
0.600
0.400
0.200
0.000
-2.000
-4.000
-6.000
-8.000
-1.000

Fig. 19

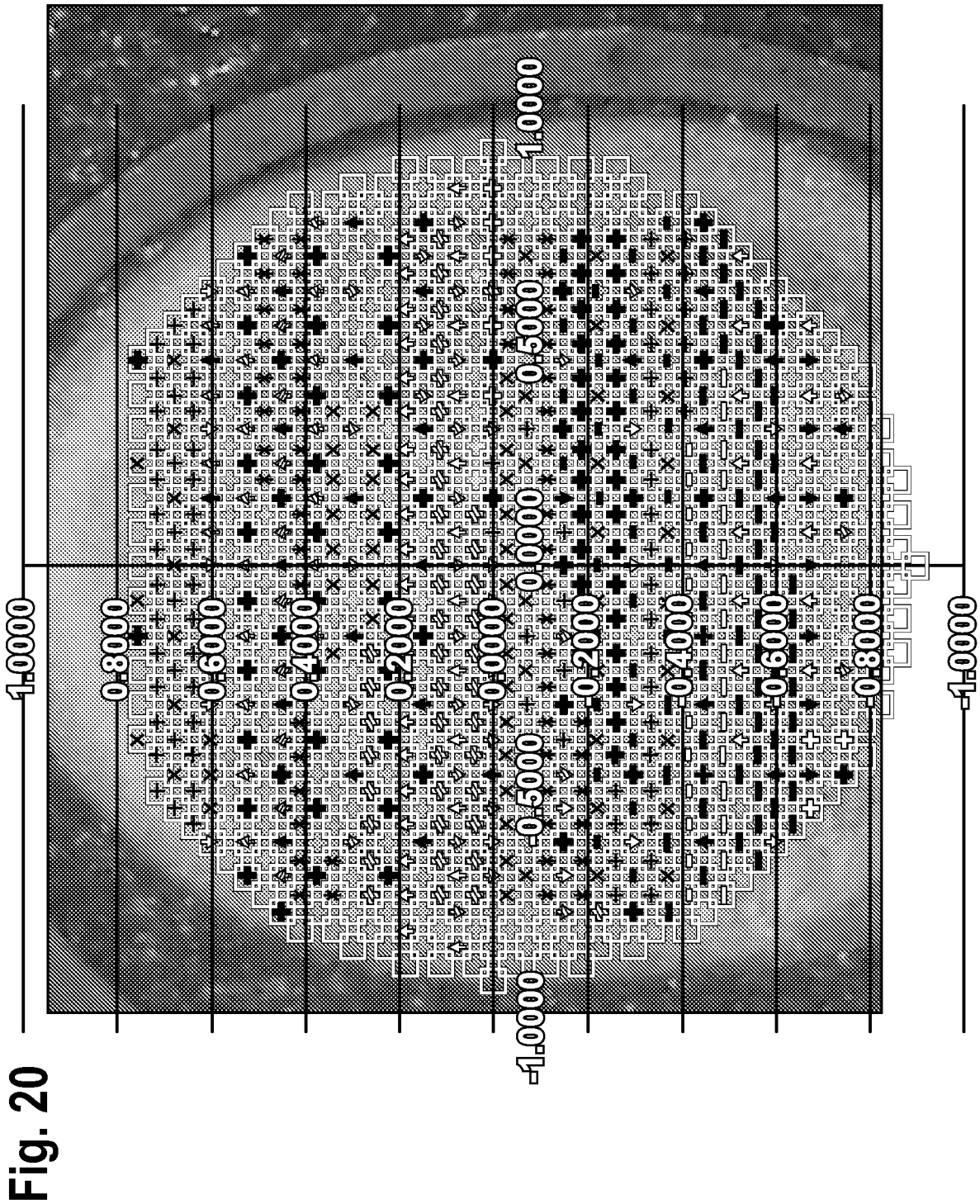
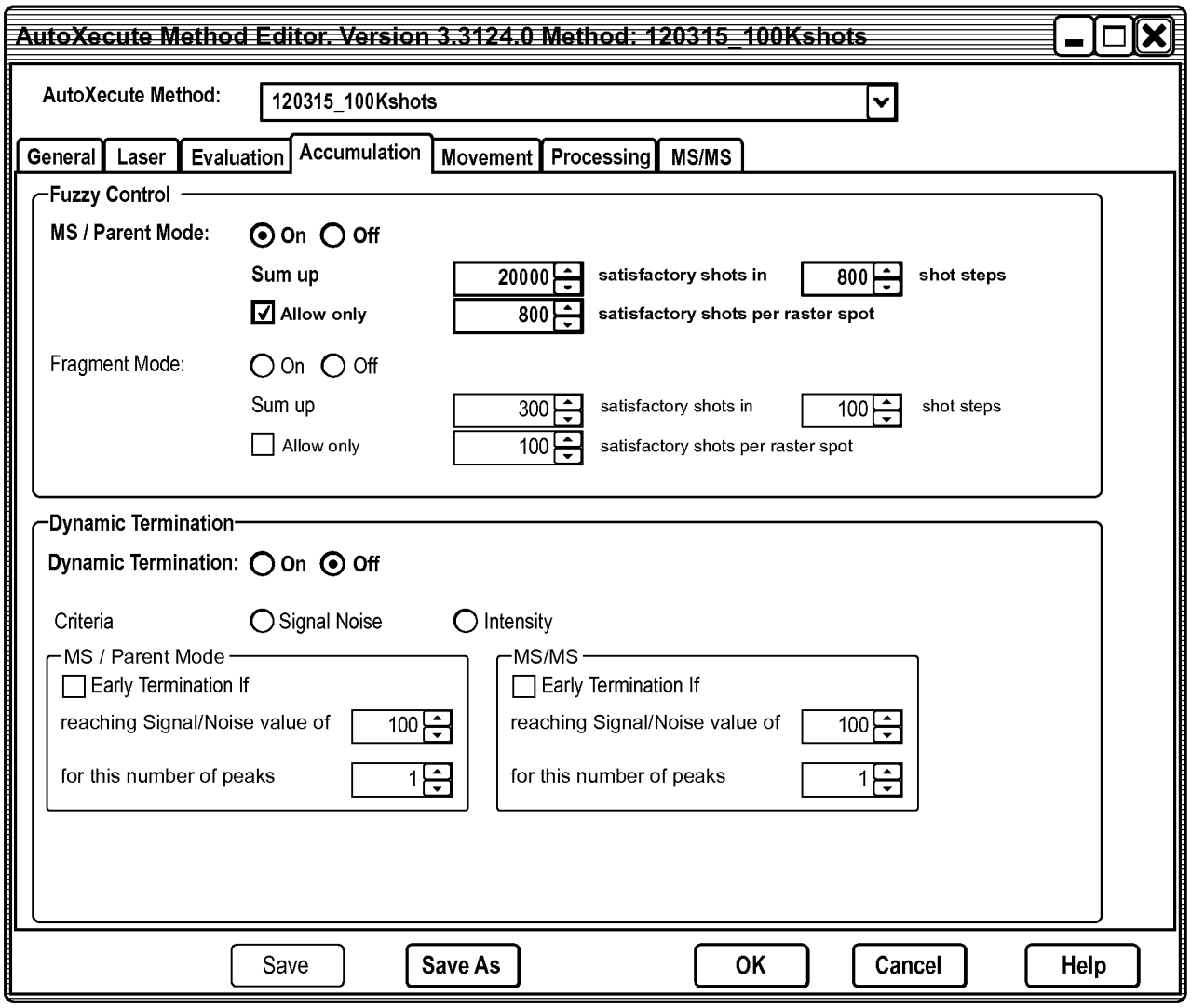

1.0000
0.8000
0.6000
0.4000
0.2000
0.0000
-0.2000
-0.4000
-0.6000
-0.8000
-1.0000
1.0000
0.5000
0.0000
-0.5000
-1.0000

Fig. 20

Fig. 21


AutoXecute Method Editor. Version 3.3124.0 Method: 120315_100Kshots
AutoXecute Method:
120315_100Kshots
General
Laser
Evaluation
Accumulation
Movement
Processing
MS/MS
Fuzzy Control
MS / Parent Mode:
On
Off
Sum up
20000
satisfactory shots in
800
shot steps
Allow only
800
satisfactory shots per raster spot
Fragment Mode:
On
Off
Sum up
300
satisfactory shots in
100
shot steps
Allow only
100
satisfactory shots per raster spot
Dynamic Termination
Dynamic Termination:
On
Off
Criteria
Signal Noise
Intensity
MS / Parent Mode
Early Termination If
reaching Signal/Noise value of
100
for this number of peaks
1
MS/MS
Early Termination If
reaching Signal/Noise value of
100
for this number of peaks
1
Save
Save As
OK
Cancel
Help

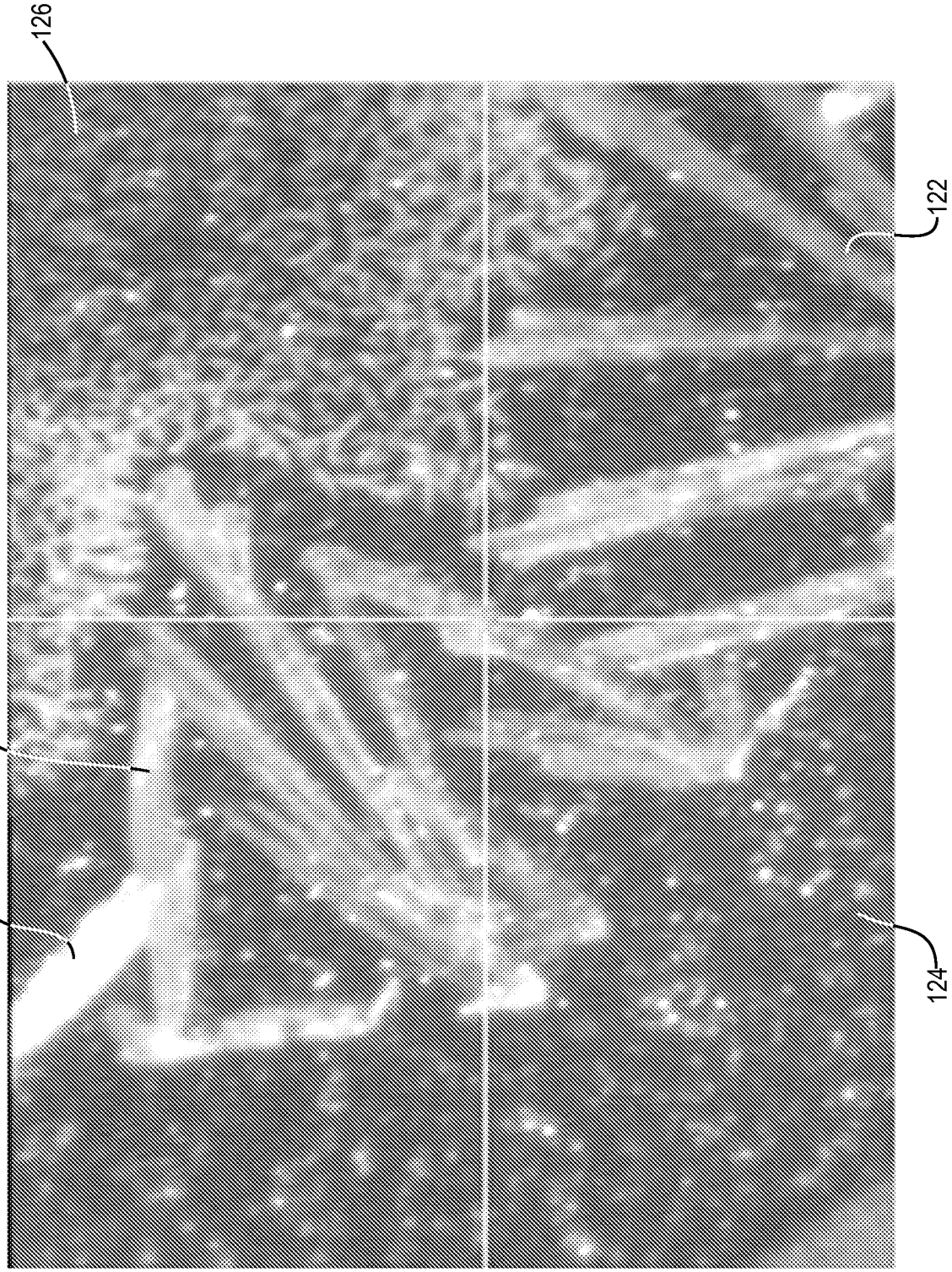


Fig. 22

Fig. 23

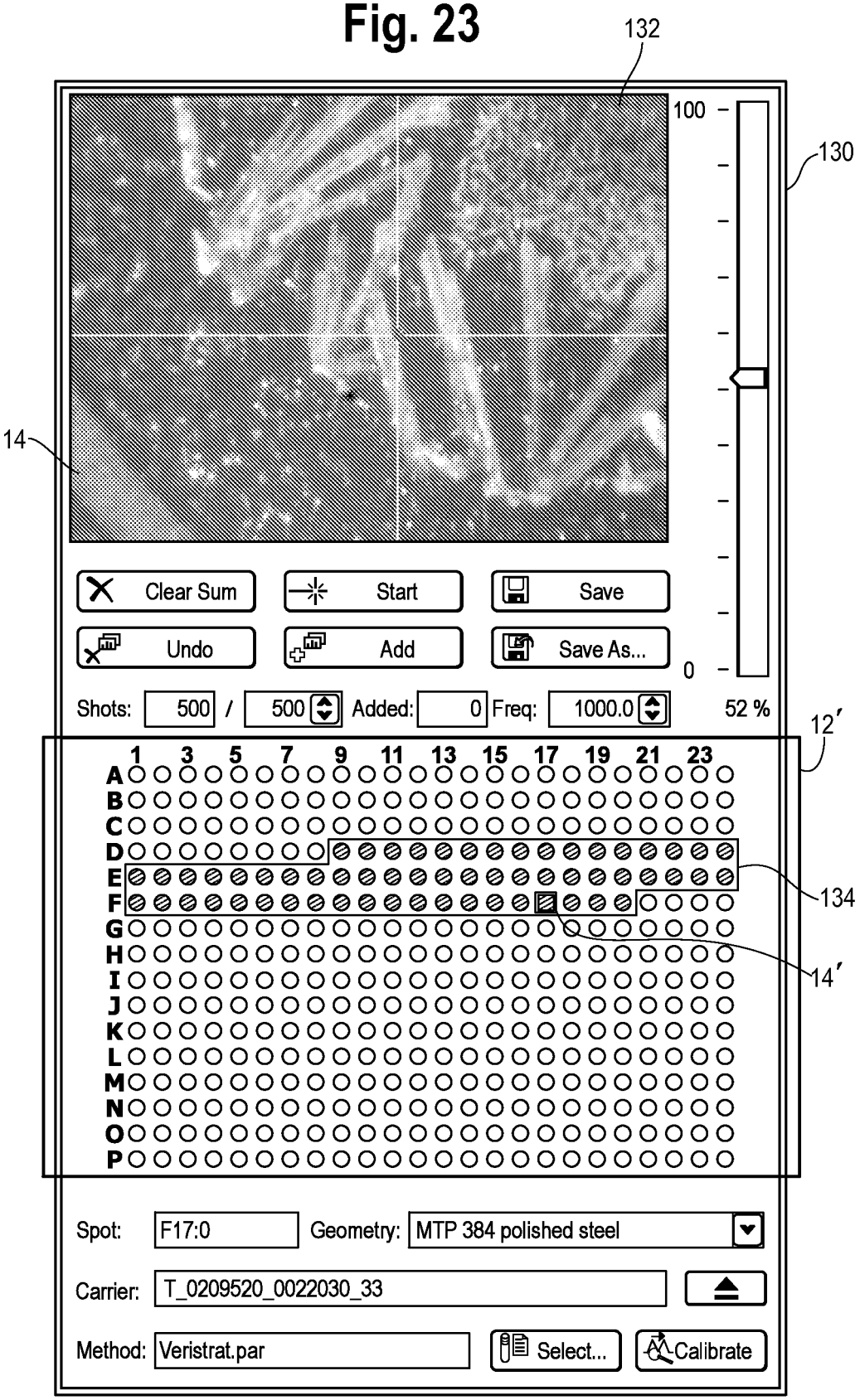

132
100
130
14
Clear Sum
Start
Save
Undo
Add
Save As...
0
Shots: 500 / 500 Added: 0 Freq: 1000.0
52 %
12′
1 3 5 7 9 11 13 15 17 19 21 23
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
134
14′
Spot: F17:0 Geometry: MTP 384 polished steel
Carrier: T_0209520_0022030_33
Method: Veristrat.par
Select...
Calibrate

Fig. 24

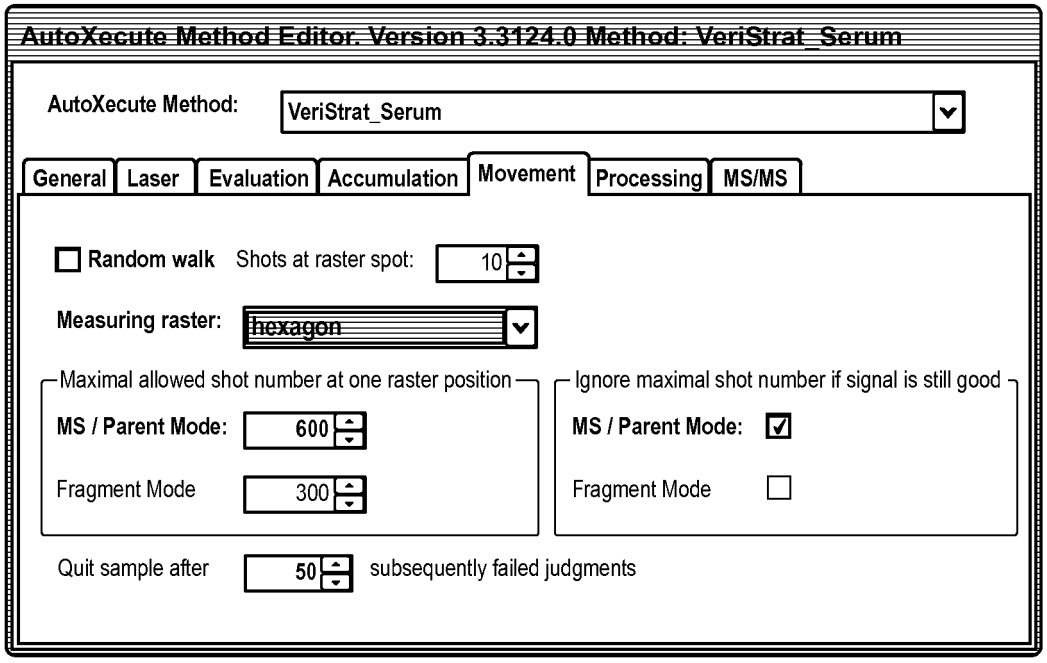

AutoXecute Method Editor. Version 3.3124.0 Method: VeriStrat_Serum
AutoXecute Method:
VeriStrat_Serum
General
Laser
Evaluation
Accumulation
Movement
Processing
MS/MS
Random walk
Shots at raster spot:
10
Measuring raster:
hexagon
Maximal allowed shot number at one raster position
MS / Parent Mode:
600
Fragment Mode
300
Ignore maximal shot number if signal is still good
MS / Parent Mode:
Fragment Mode
Quit sample after
50
subsequently failed judgments

Fig. 25

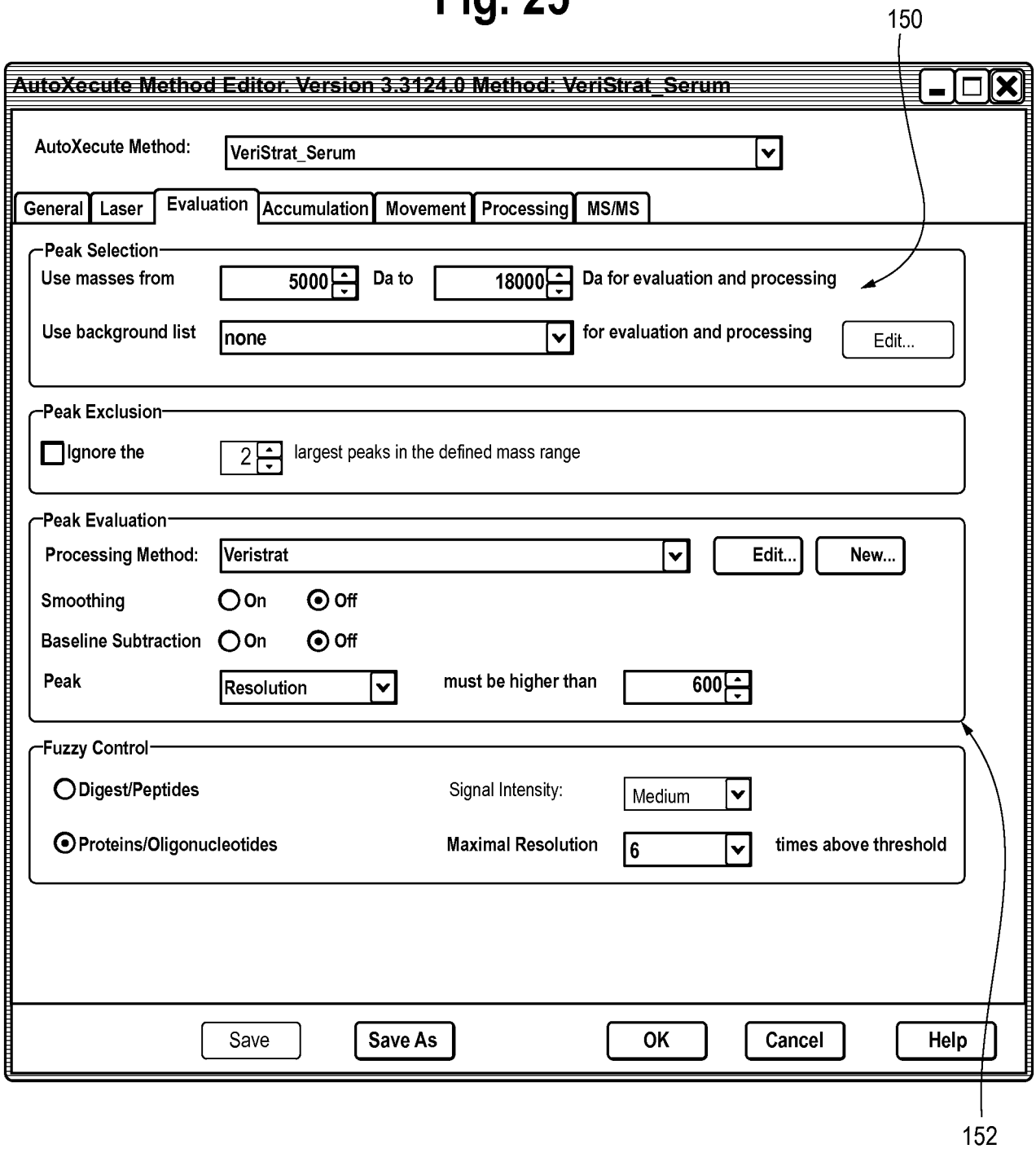
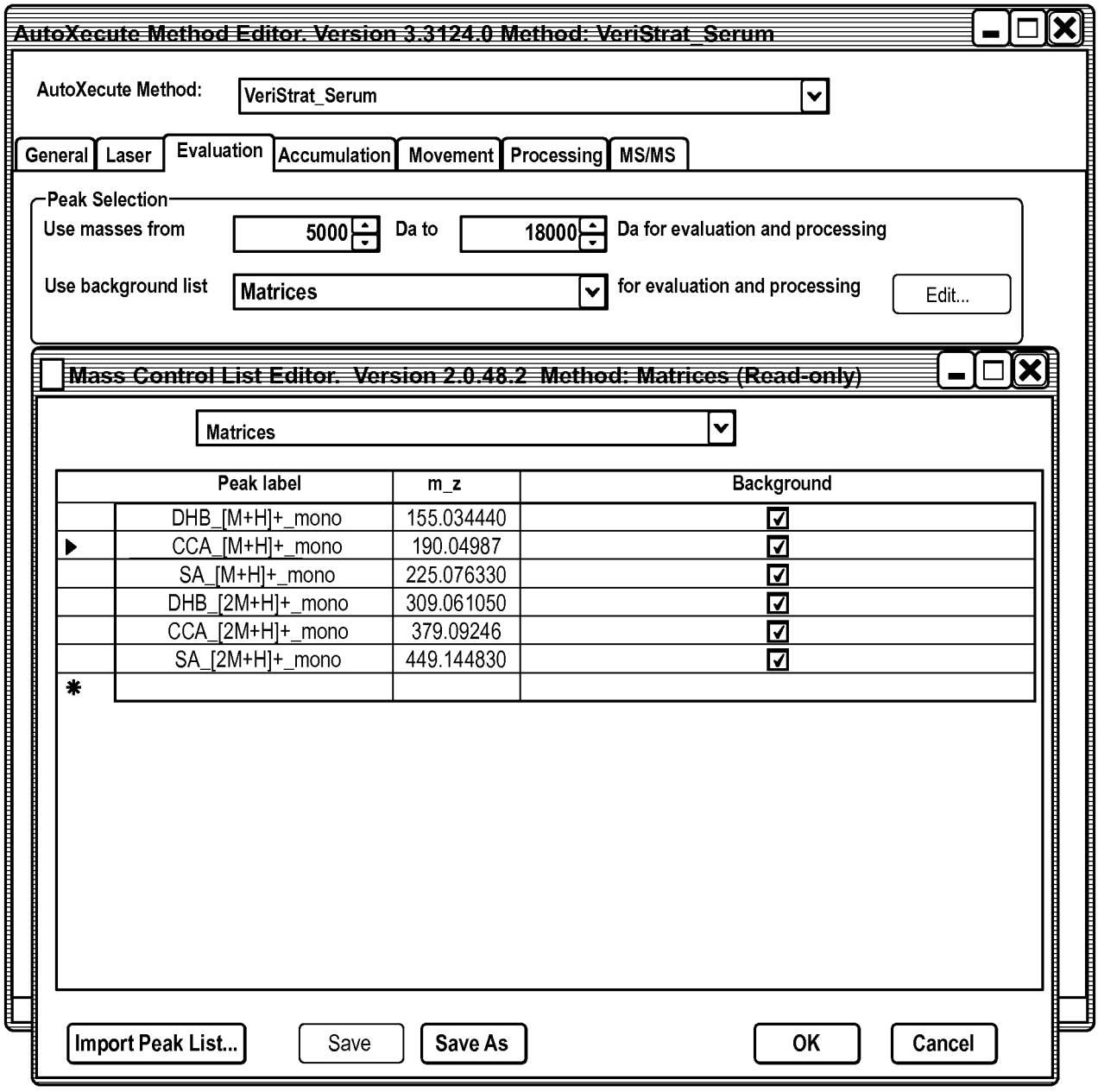

150
AutoXecute Method Editor. Version 3.3124.0 Method: VeriStrat_Serum
AutoXecute Method:
VeriStrat_Serum
General
Laser
Evaluation
Accumulation
Movement
Processing
MS/MS
Peak Selection
Use masses from
5000
Da to
18000
Da for evaluation and processing
Use background list
none
for evaluation and processing
Edit...
Peak Exclusion
Ignore the
2
largest peaks in the defined mass range
Peak Evaluation
Processing Method:
Veristrat
Edit...
New...
Smoothing
On
Off
Baseline Subtraction
On
Off
Peak
Resolution
must be higher than
600
Fuzzy Control
Digest/Peptides
Signal Intensity:
Medium
Proteins/Oligonucleotides
Maximal Resolution
6
times above threshold
Save
Save As
OK
Cancel
Help
152

Fig. 26


AutoXecute Method Editor. Version 3.3124.0 Method: VeriStrat_Serum
AutoXecute Method:
VeriStrat_Serum
General
Laser
Evaluation
Accumulation
Movement
Processing
MS/MS
Peak Selection
Use masses from
5000
Da to
18000
Da for evaluation and processing
Use background list
Matrices
for evaluation and processing
Edit...
Mass Control List Editor. Version 2.0.48.2 Method: Matrices (Read-only)
Matrices
Peak label
m_z
Background
DHB_[M+H]+_mono
155.034440
CCA_[M+H]+_mono
190.04987
SA_[M+H]+_mono
225.076330
DHB_[2M+H]+_mono
309.061050
CCA_[2M+H]+_mono
379.09246
SA_[2M+H]+_mono
449.144830
Import Peak List...
Save
Save As
OK
Cancel