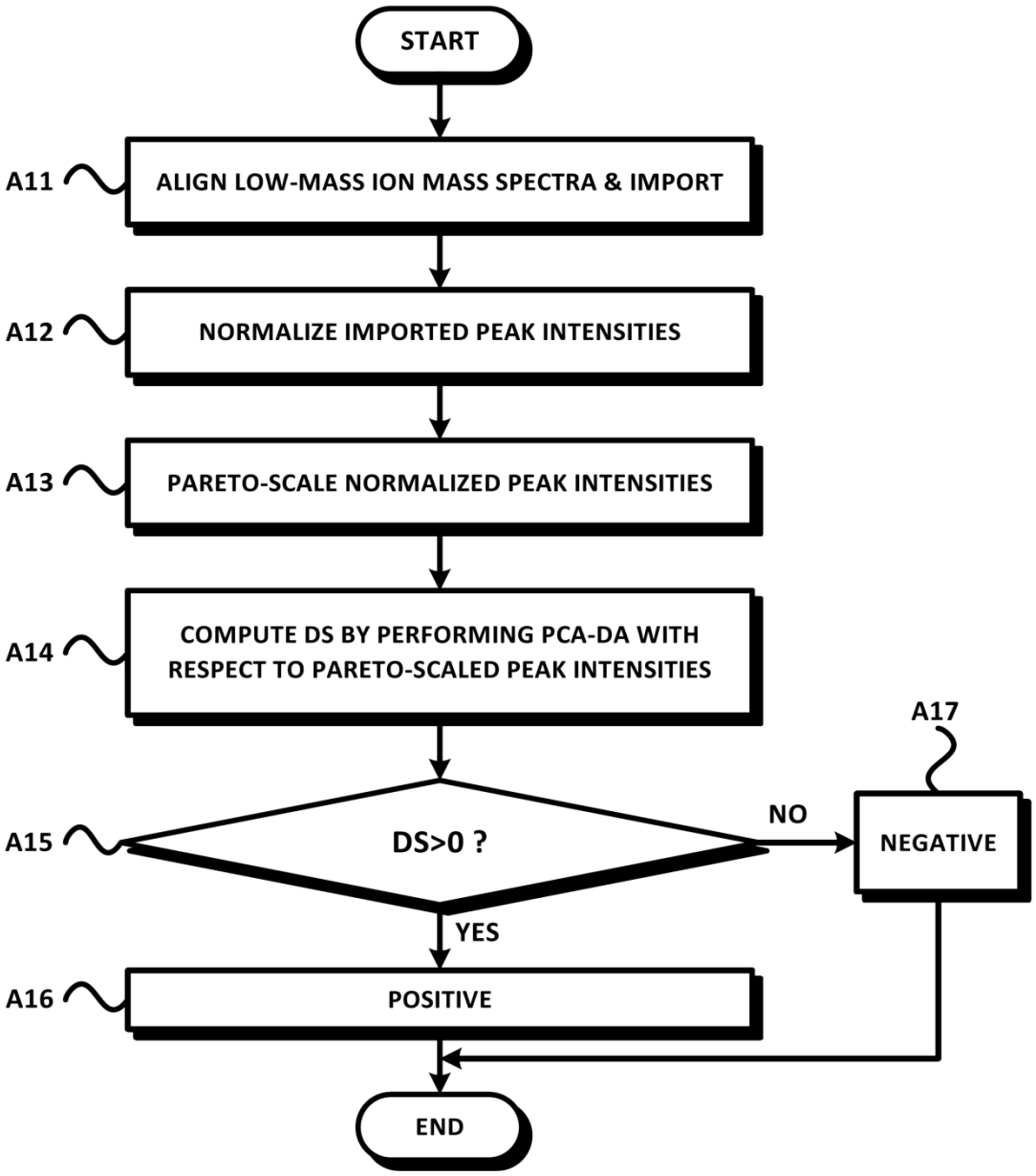

START
A11
ALIGN LOW-MASS ION MASS SPECTRA & IMPORT
A12
NORMALIZE IMPORTED PEAK INTENSITIES
A13
PARETO-SCALE NORMALIZED PEAK INTENSITIES
A14
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
A17
A15
DS>0 ?
NO
NEGATIVE
YES
A16
POSITIVE
END

FIG. 1

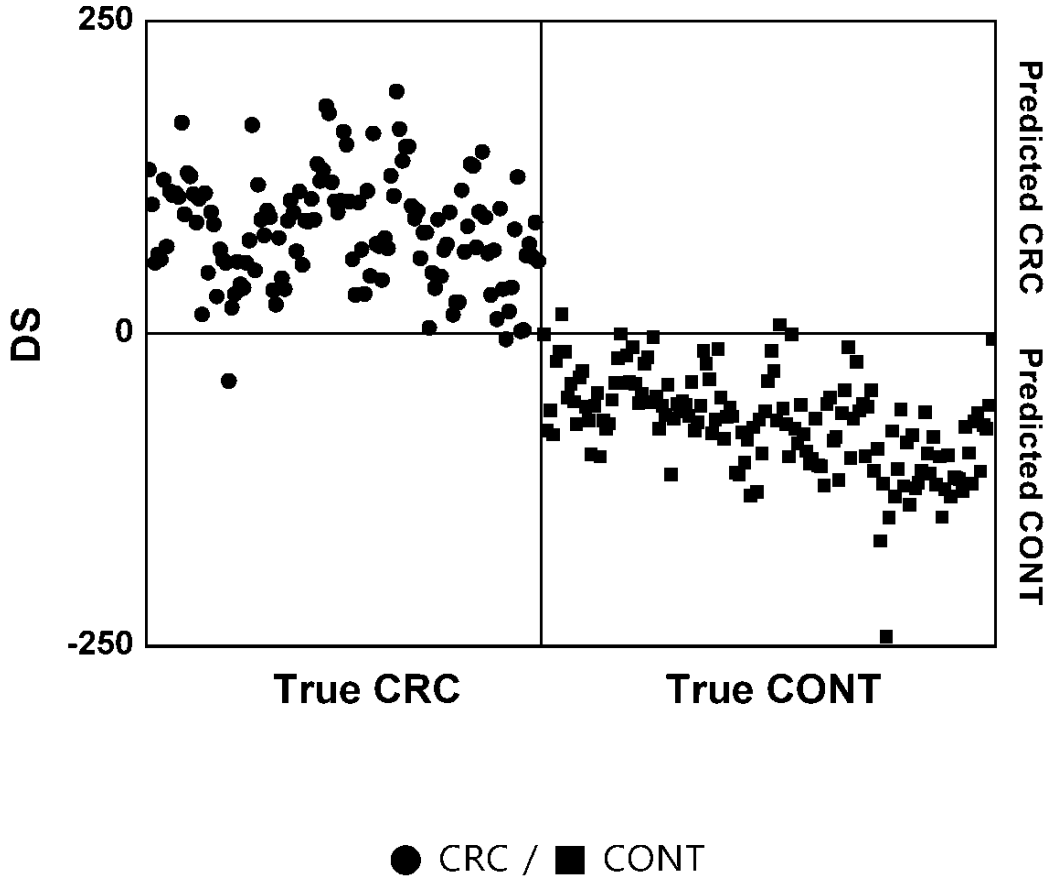

250
0
-250
DS
True CRC
True CONT
Predicted CRC
Predicted CONT
● CRC / ■ CONT

FIG. 2

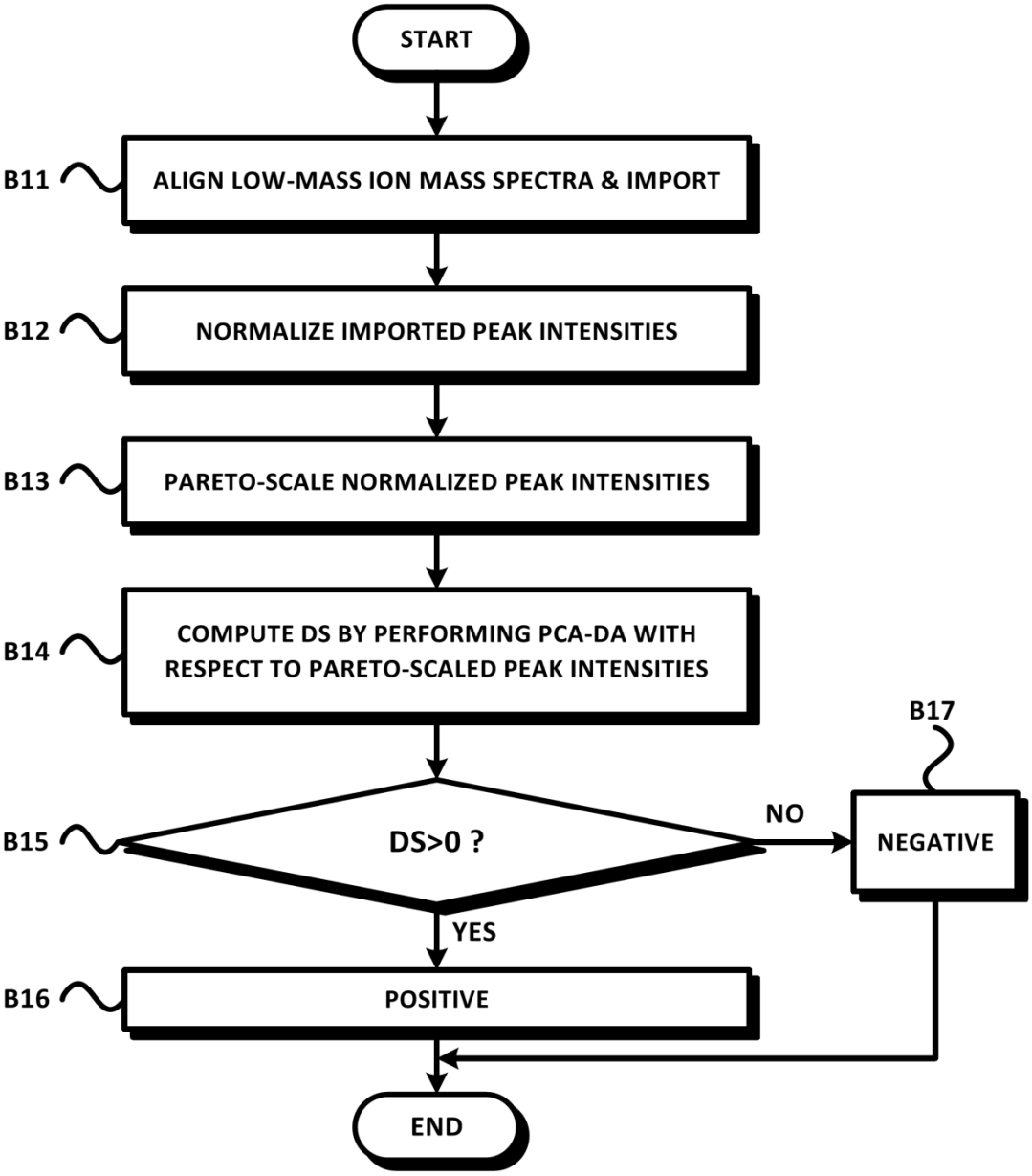

START
B11
ALIGN LOW-MASS ION MASS SPECTRA & IMPORT
B12
NORMALIZE IMPORTED PEAK INTENSITIES
B13
PARETO-SCALE NORMALIZED PEAK INTENSITIES
B14
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
B15
DS>0 ?
NO
B17
NEGATIVE
YES
B16
POSITIVE
END

FIG. 3

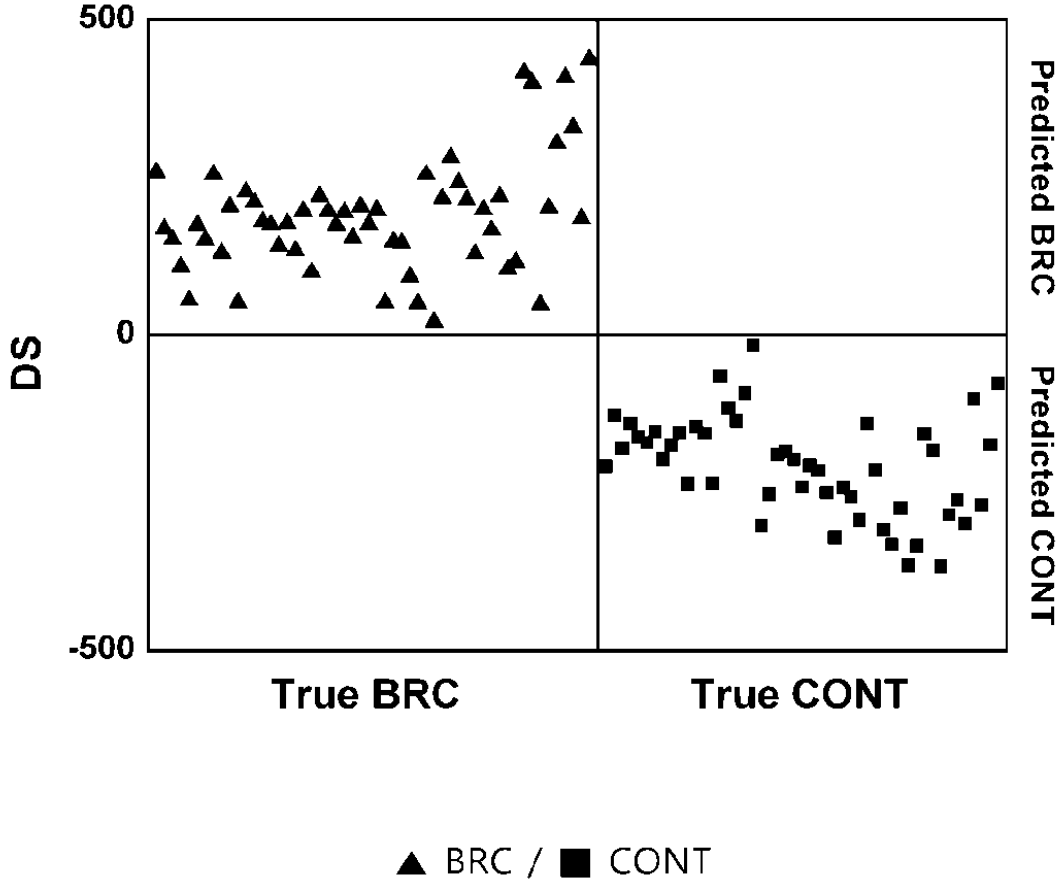

500
0
-500
DS
Predicted BRC
Predicted CONT
True BRC
True CONT
▲ BRC / ■ CONT

FIG. 4

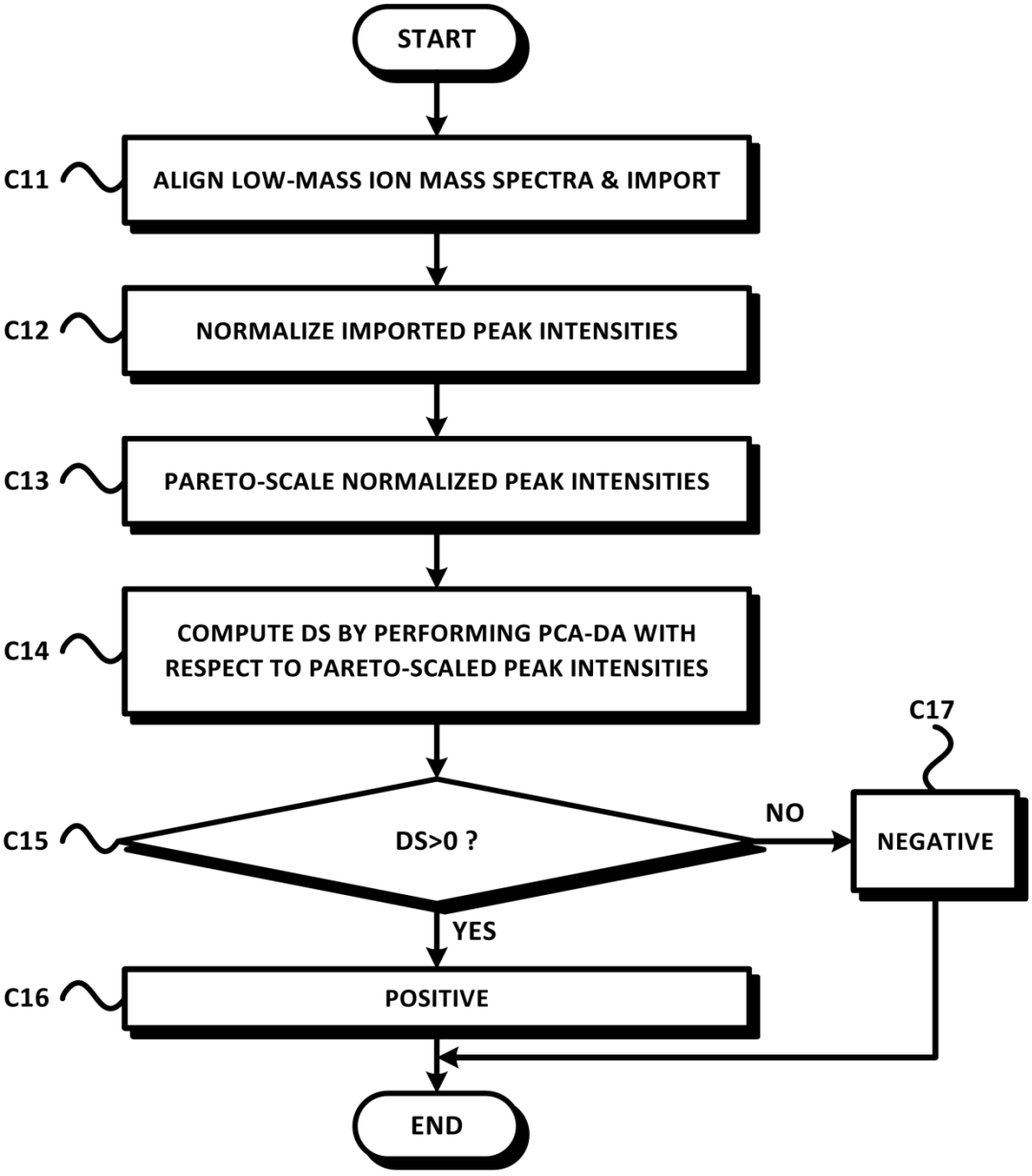

START
C11
ALIGN LOW-MASS ION MASS SPECTRA & IMPORT
C12
NORMALIZE IMPORTED PEAK INTENSITIES
C13
PARETO-SCALE NORMALIZED PEAK INTENSITIES
C14
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
C15
DS>0 ?
NO
C17
NEGATIVE
YES
C16
POSITIVE
END

FIG. 5

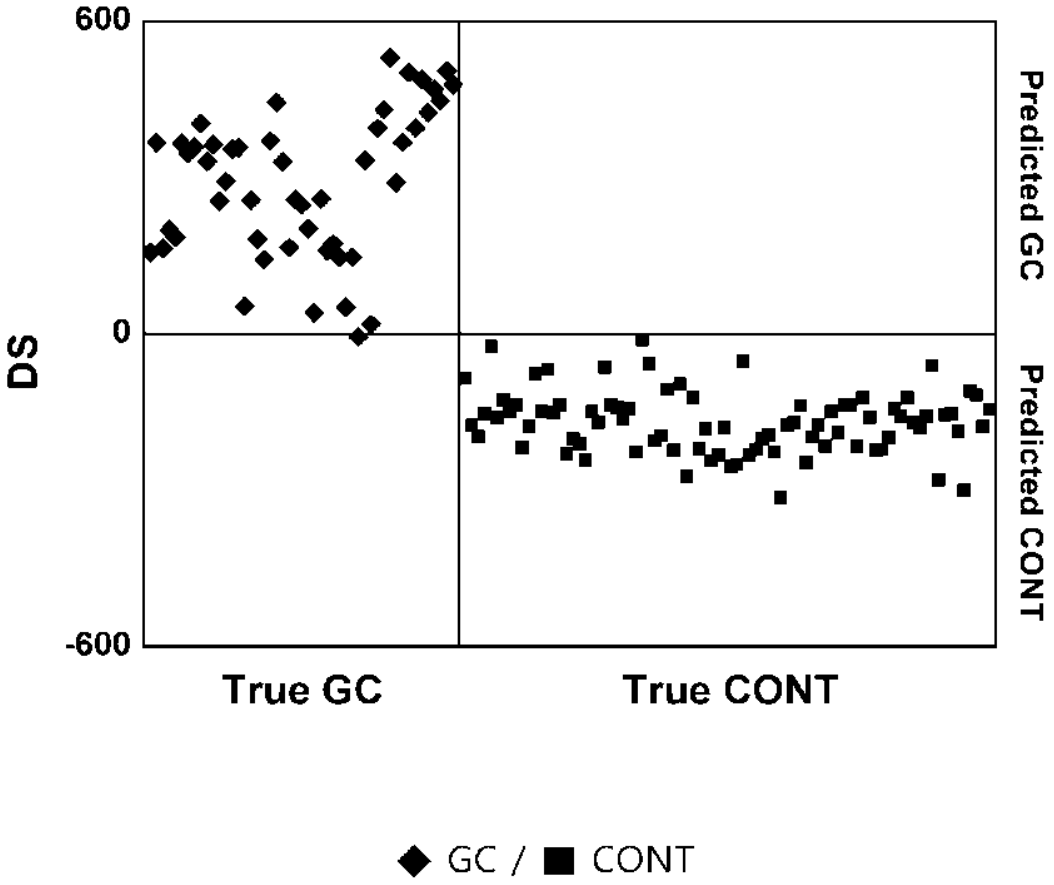

600
0
-600
DS
True GC
True CONT
Predicted GC
Predicted CONT
◆ GC / ■ CONT

FIG. 6

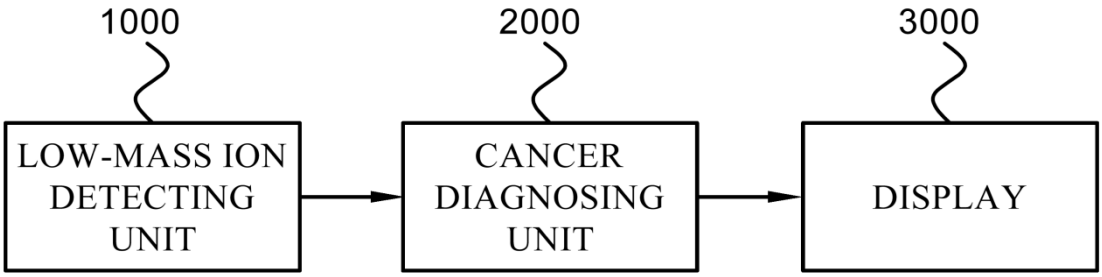

1000
2000
3000
LOW-MASS ION DETECTING UNIT
CANCER DIAGNOSING UNIT
DISPLAY

FIG. 7

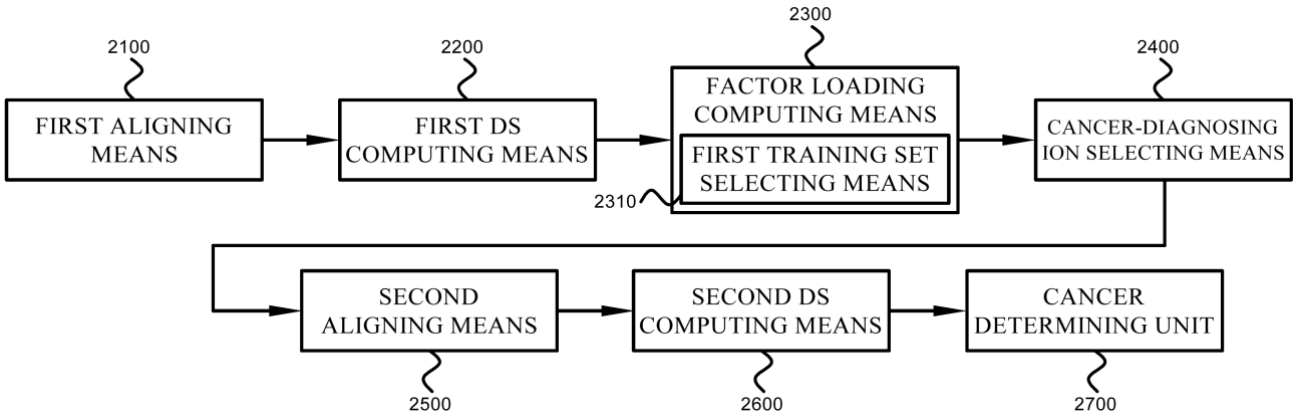

2100
FIRST ALIGNING MEANS
2200
FIRST DS COMPUTING MEANS
2300
FACTOR LOADING COMPUTING MEANS
FIRST TRAINING SET SELECTING MEANS
2310
2400
CANCER-DIAGNOSING ION SELECTING MEANS
SECOND ALIGNING MEANS
2500
SECOND DS COMPUTING MEANS
2600
CANCER DETERMINING UNIT
2700

FIG. 8

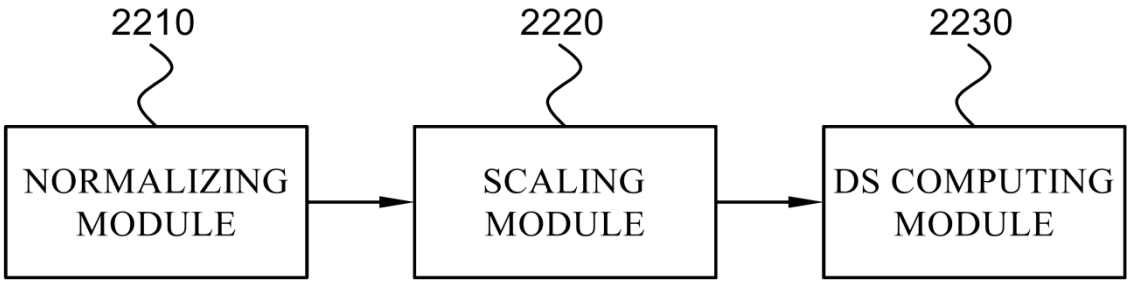

2210
2220
2230
NORMALIZING MODULE
SCALING MODULE
DS COMPUTING MODULE

FIG. 9

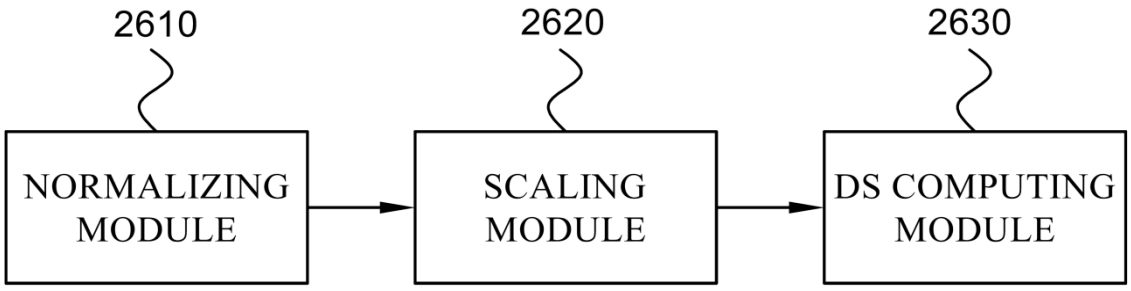

2610
2620
2630
NORMALIZING MODULE
SCALING MODULE
DS COMPUTING MODULE

FIG. 10

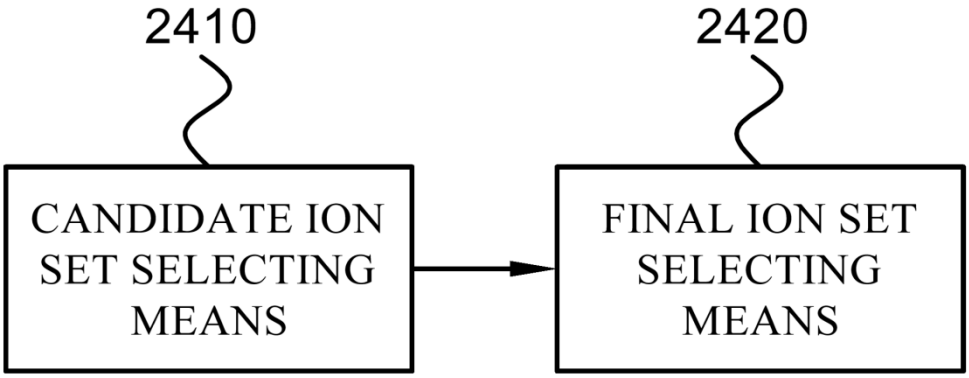

2410
2420
CANDIDATE ION SET SELECTING MEANS
FINAL ION SET SELECTING MEANS

FIG. 11

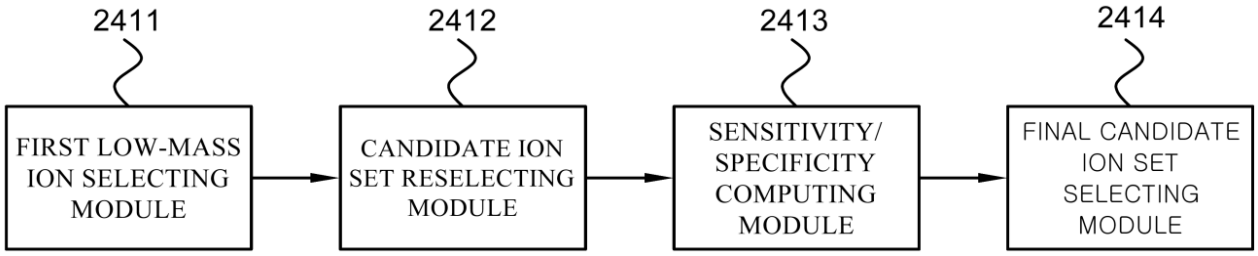

2411
2412
2413
2414
FIRST LOW-MASS ION SELECTING MODULE
CANDIDATE ION SET RESELECTING MODULE
SENSITIVITY/ SPECIFICITY COMPUTING MODULE
FINAL CANDIDATE ION SET SELECTING MODULE

FIG. 12

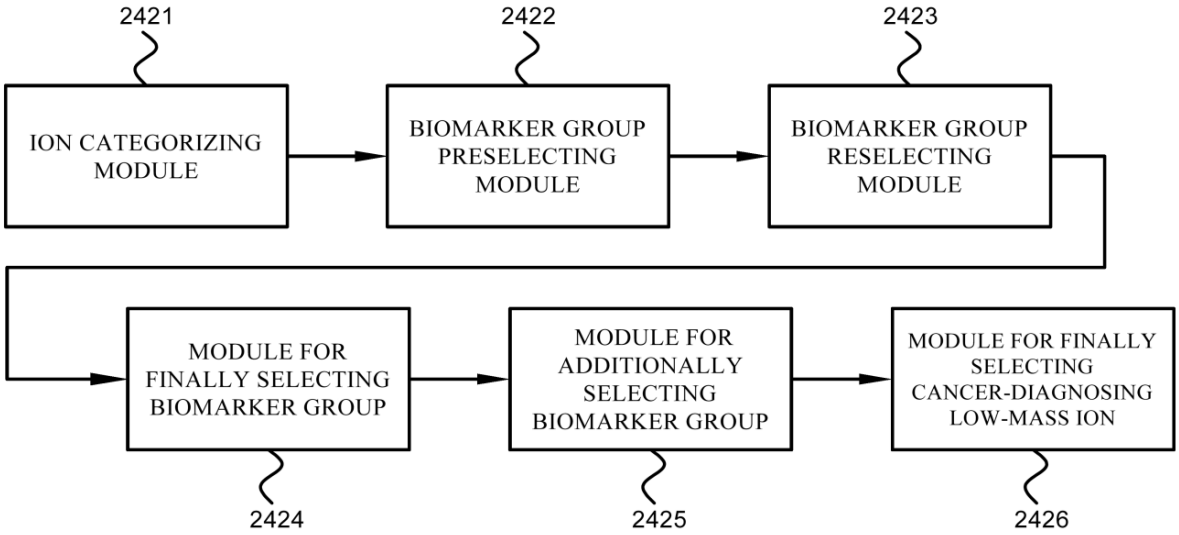

2421
ION CATEGORIZING MODULE
2422
BIOMARKER GROUP PRESELECTING MODULE
2423
BIOMARKER GROUP RESELECTING MODULE
MODULE FOR FINALLY SELECTING BIOMARKER GROUP
MODULE FOR ADDITIONALLY SELECTING BIOMARKER GROUP
MODULE FOR FINALLY SELECTING CANCER-DIAGNOSING LOW-MASS ION
2424
2425
2426

FIG. 13

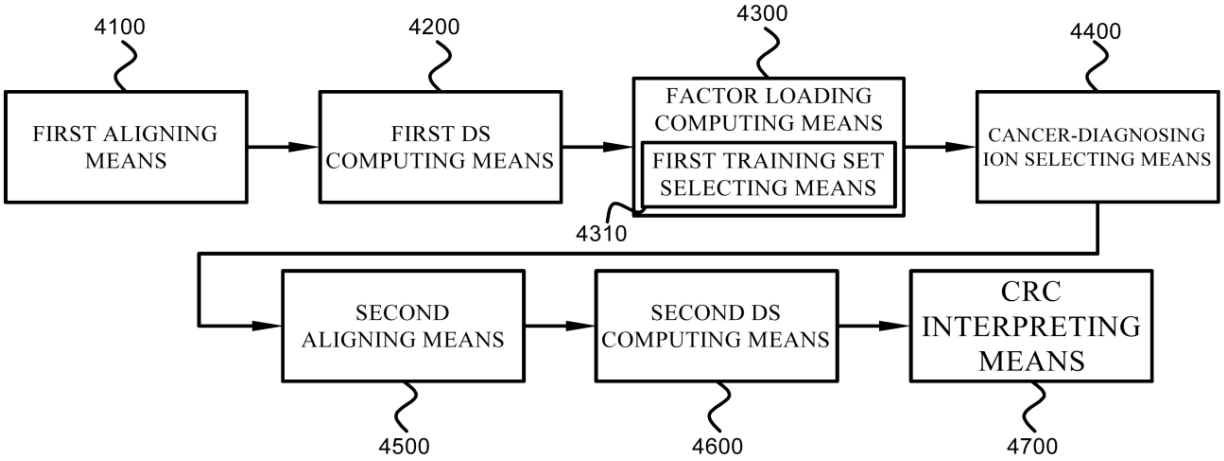

4100
FIRST ALIGNING MEANS
4200
FIRST DS COMPUTING MEANS
4300
FACTOR LOADING COMPUTING MEANS
FIRST TRAINING SET SELECTING MEANS
4310
4400
CANCER-DIAGNOSING ION SELECTING MEANS
SECOND ALIGNING MEANS
4500
SECOND DS COMPUTING MEANS
4600
CRC INTERPRETING MEANS
4700

FIG. 14

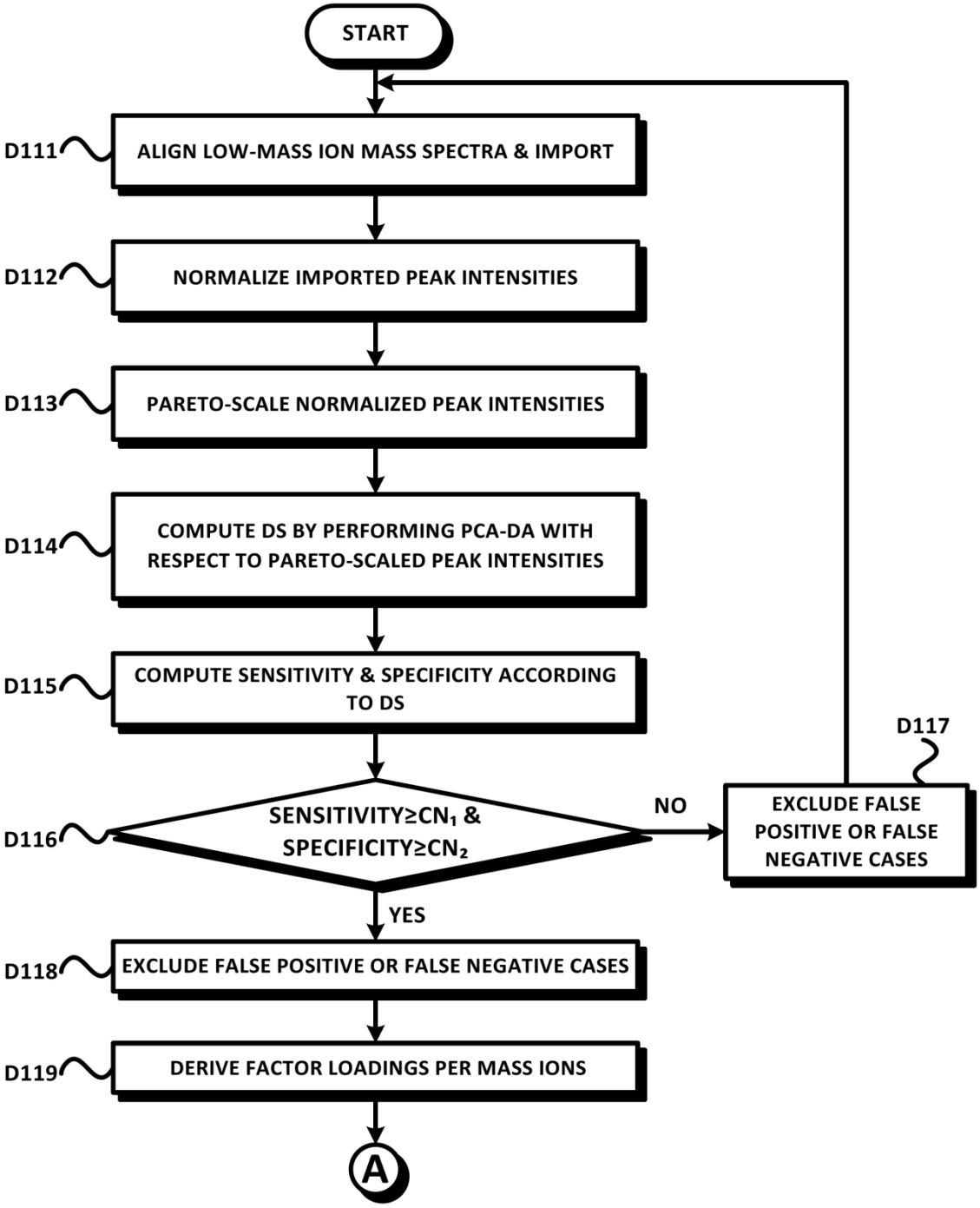

START
D111
ALIGN LOW-MASS ION MASS SPECTRA & IMPORT
D112
NORMALIZE IMPORTED PEAK INTENSITIES
D113
PARETO-SCALE NORMALIZED PEAK INTENSITIES
D114
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
D115
COMPUTE SENSITIVITY & SPECIFICITY ACCORDING TO DS
D116
SENSITIVITY≥CN1 & SPECIFICITY≥CN2
NO
D117
EXCLUDE FALSE POSITIVE OR FALSE NEGATIVE CASES
YES
D118
EXCLUDE FALSE POSITIVE OR FALSE NEGATIVE CASES
D119
DERIVE FACTOR LOADINGS PER MASS IONS
A

FIG. 15

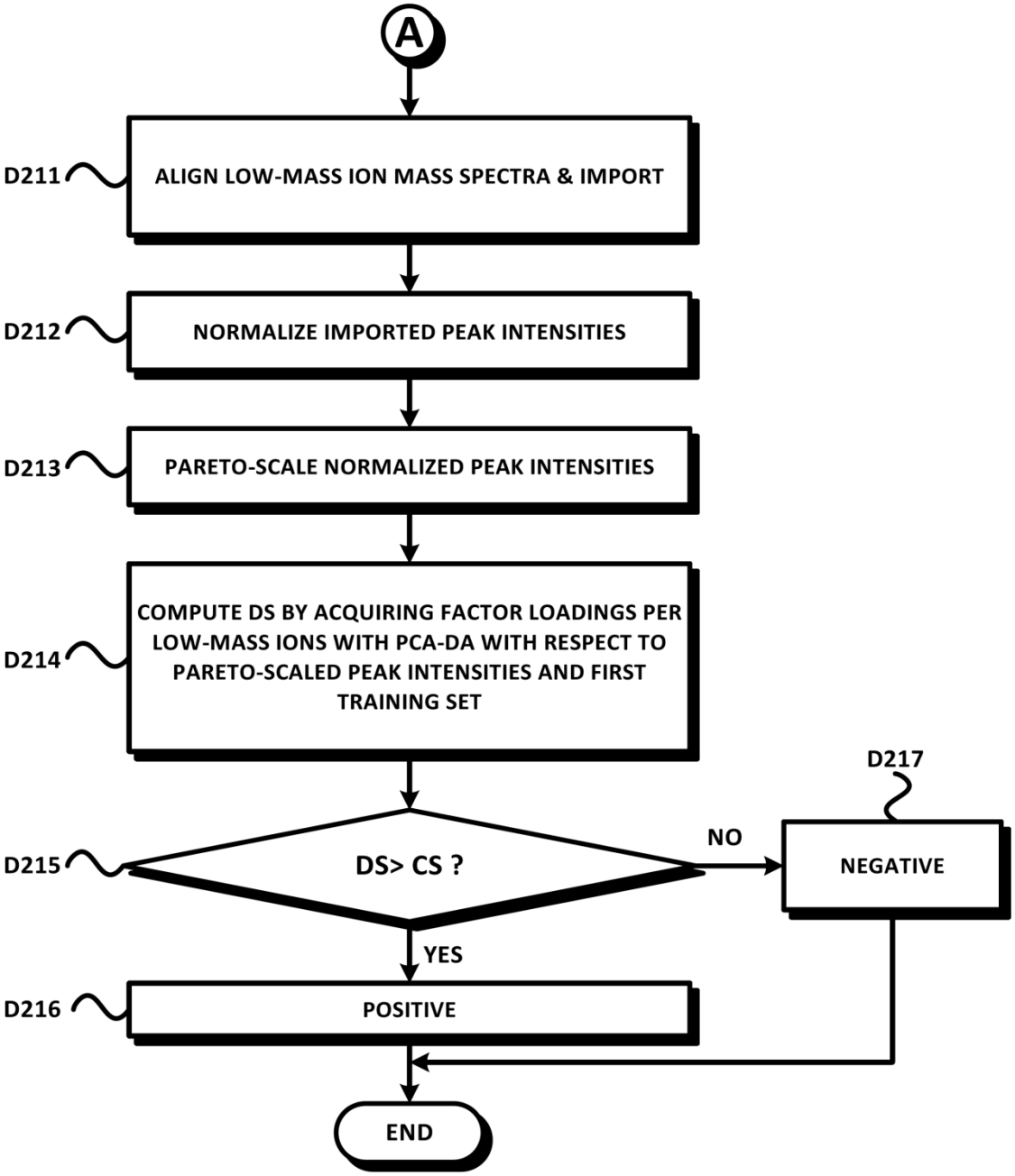

A
D211
ALIGN LOW-MASS ION MASS SPECTRA & IMPORT
D212
NORMALIZE IMPORTED PEAK INTENSITIES
D213
PARETO-SCALE NORMALIZED PEAK INTENSITIES
D214
COMPUTE DS BY ACQUIRING FACTOR LOADINGS PER LOW-MASS IONS WITH PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES AND FIRST TRAINING SET
D215
DS> CS ?
NO
D217
NEGATIVE
YES
D216
POSITIVE
END

FIG. 16

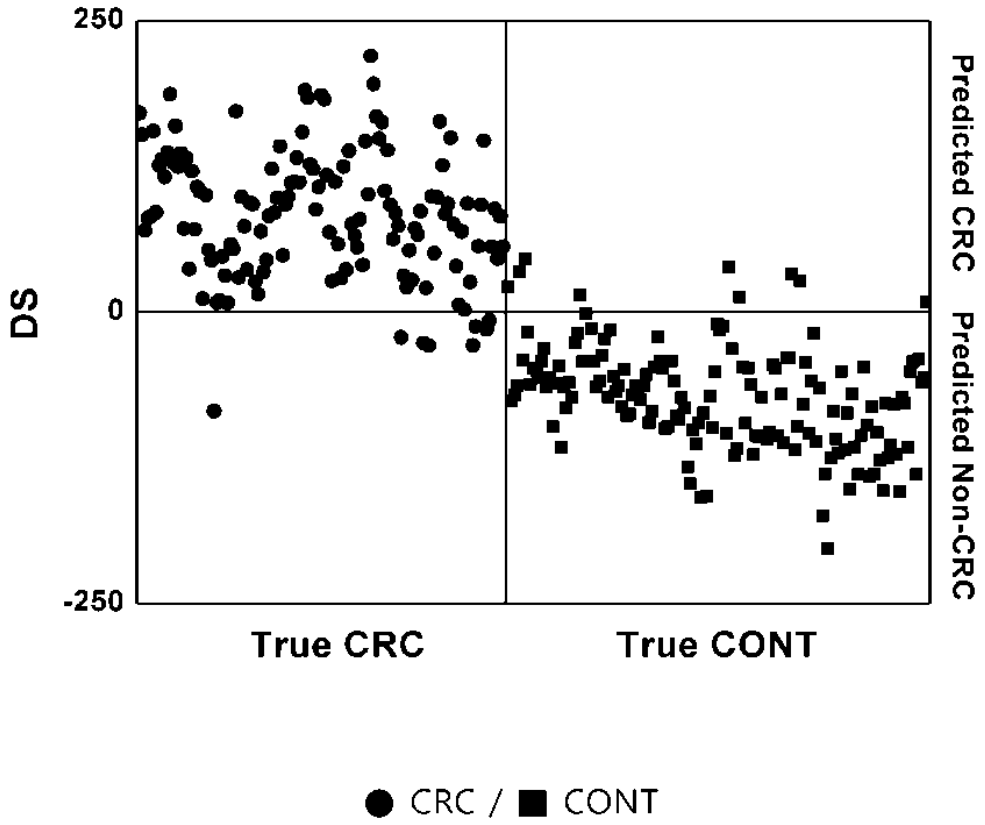

250
0
-250
DS
True CRC
True CONT
Predicted CRC
Predicted Non-CRC
● CRC / ■ CONT

FIG. 17

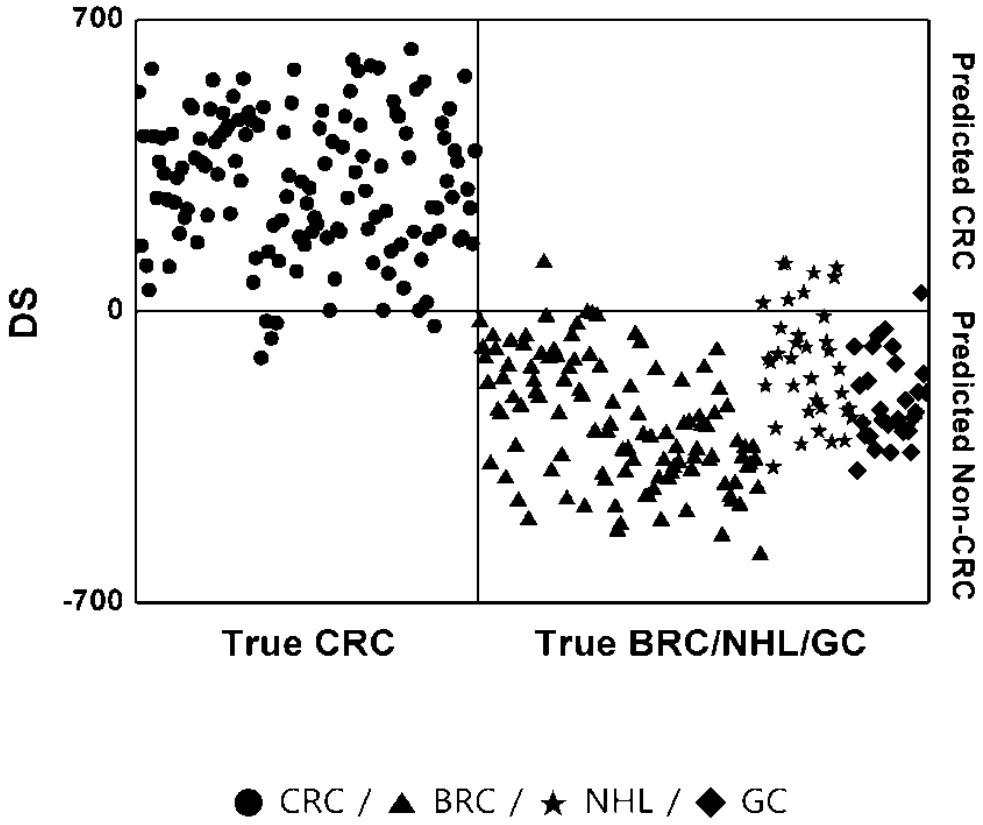

700
0
-700
DS
True CRC
True BRC/NHL/GC
Predicted CRC
Predicted Non-CRC
● CRC / ▲ BRC / ★ NHL / ◆ GC

FIG. 18

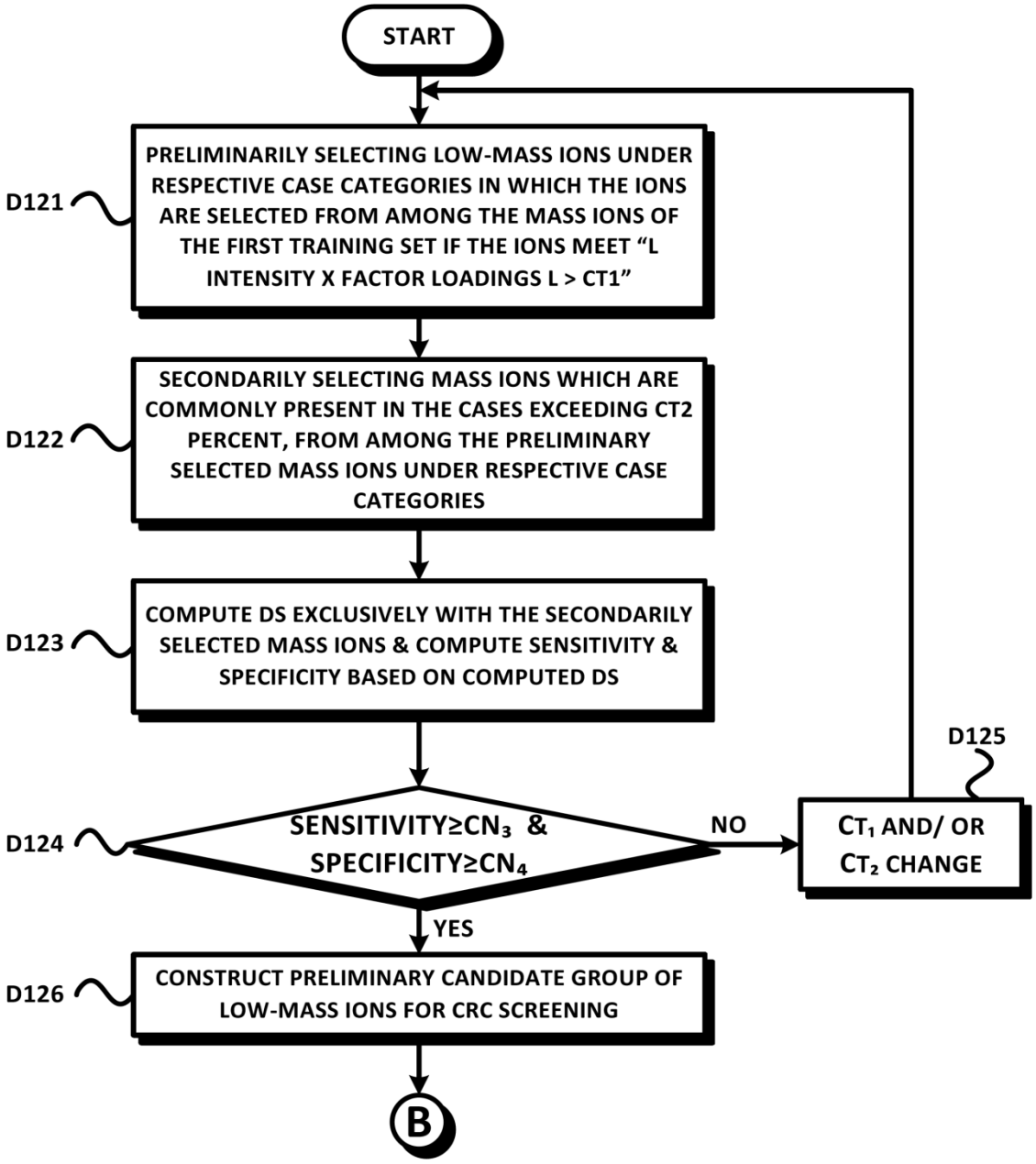

START
PRELIMINARILY SELECTING LOW-MASS IONS UNDER RESPECTIVE CASE CATEGORIES IN WHICH THE IONS ARE SELECTED FROM AMONG THE MASS IONS OF THE FIRST TRAINING SET IF THE IONS MEET "L INTENSITY X FACTOR LOADINGS L > CT1"
D121
SECONDARILY SELECTING MASS IONS WHICH ARE COMMONLY PRESENT IN THE CASES EXCEEDING CT2 PERCENT, FROM AMONG THE PRELIMINARY SELECTED MASS IONS UNDER RESPECTIVE CASE CATEGORIES
D122
COMPUTE DS EXCLUSIVELY WITH THE SECONDARILY SELECTED MASS IONS & COMPUTE SENSITIVITY & SPECIFICITY BASED ON COMPUTED DS
D123
SENSITIVITY≥CN3 & SPECIFICITY≥CN4
D124
NO
CT1 AND/ OR CT2 CHANGE
D125
YES
CONSTRUCT PRELIMINARY CANDIDATE GROUP OF LOW-MASS IONS FOR CRC SCREENING
D126
B

FIG. 19

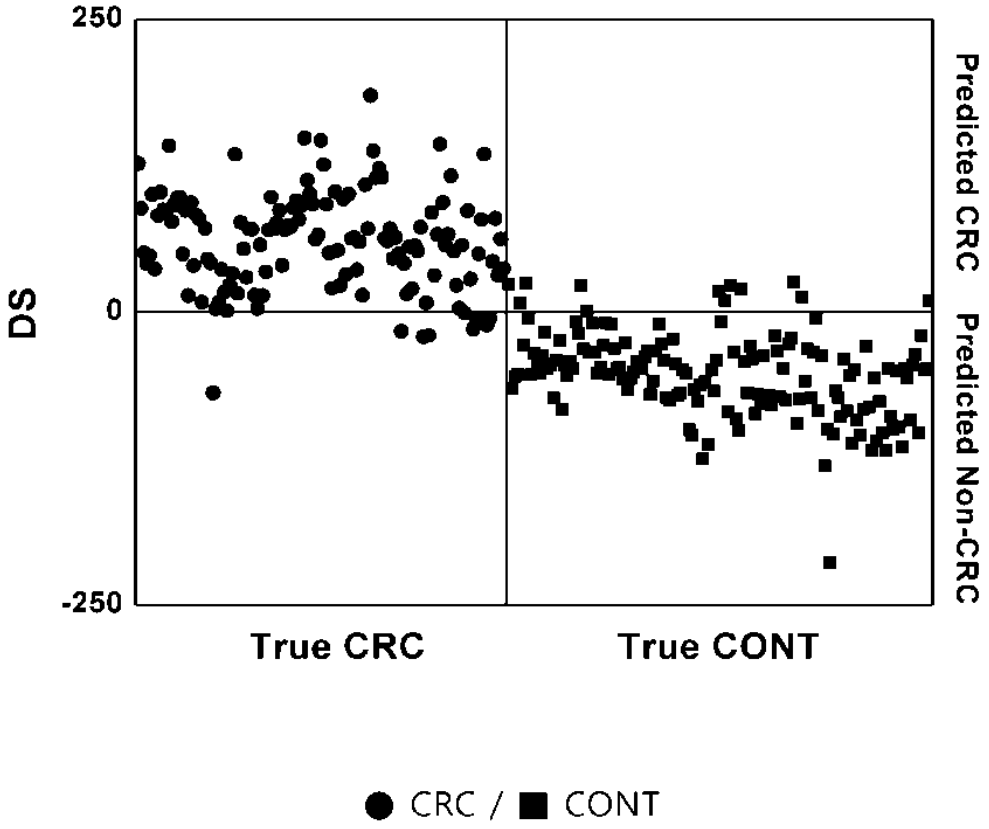

250
0
-250
DS
True CRC
True CONT
Predicted CRC
Predicted Non-CRC
● CRC / ■ CONT

FIG. 20

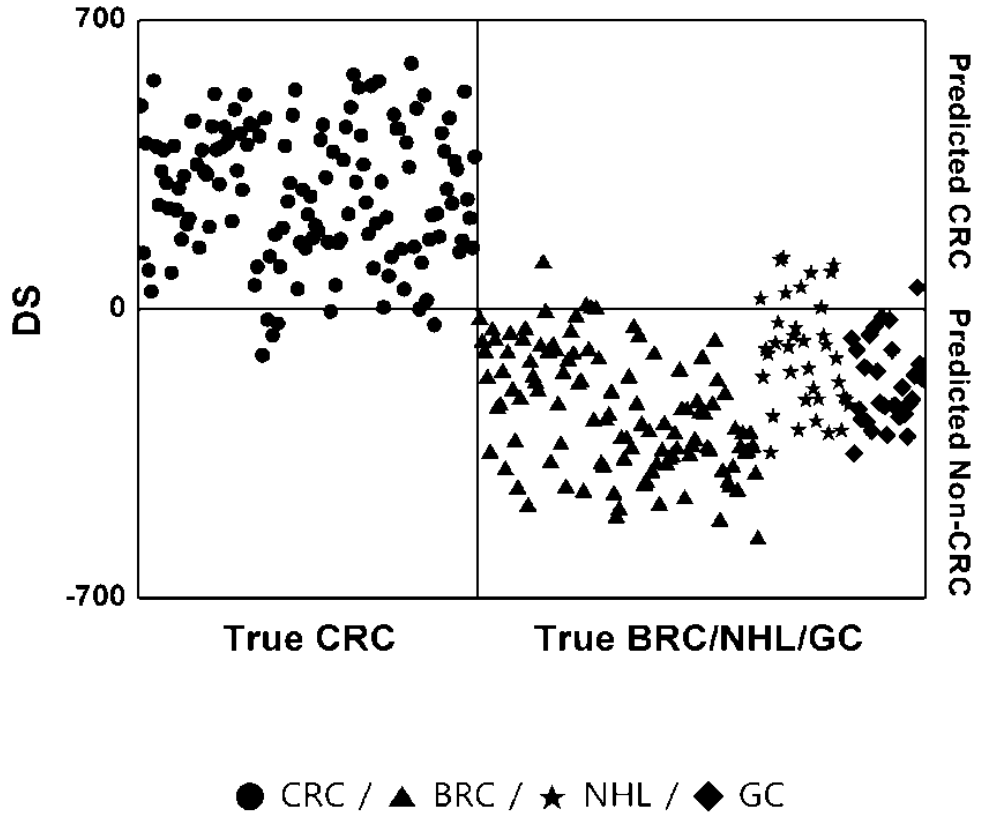

700
0
-700
DS
Predicted CRC
Predicted Non-CRC
True CRC
True BRC/NHL/GC
● CRC / ▲ BRC / ★ NHL / ◆ GC

FIG. 21

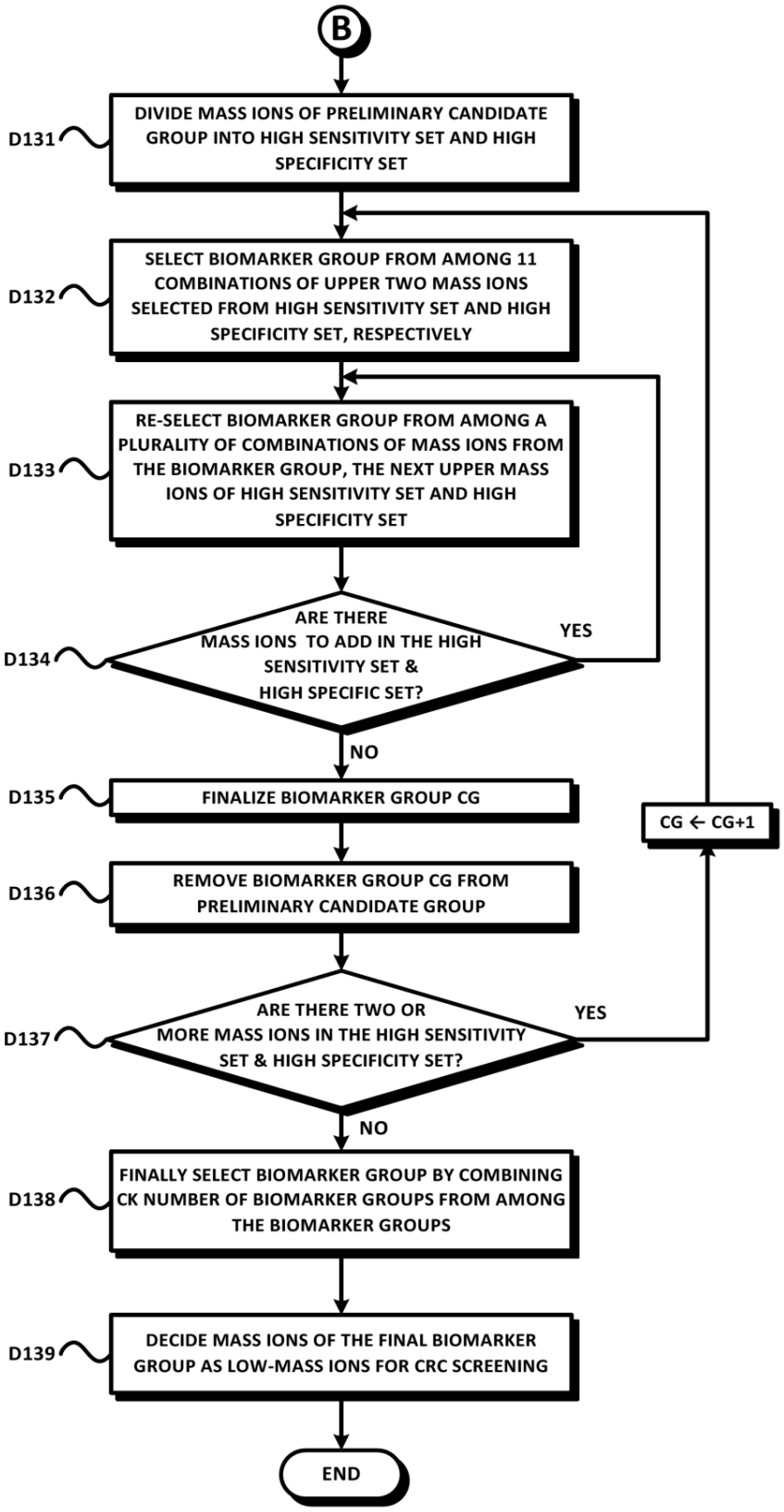

B
D131
DIVIDE MASS IONS OF PRELIMINARY CANDIDATE GROUP INTO HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
D132
SELECT BIOMARKER GROUP FROM AMONG 11 COMBINATIONS OF UPPER TWO MASS IONS SELECTED FROM HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET, RESPECTIVELY
D133
RE-SELECT BIOMARKER GROUP FROM AMONG A PLURALITY OF COMBINATIONS OF MASS IONS FROM THE BIOMARKER GROUP, THE NEXT UPPER MASS IONS OF HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
D134
ARE THERE MASS IONS TO ADD IN THE HIGH SENSITIVITY SET & HIGH SPECIFIC SET?
YES
NO
D135
FINALIZE BIOMARKER GROUP CG
CG ← CG+1
D136
REMOVE BIOMARKER GROUP CG FROM PRELIMINARY CANDIDATE GROUP
D137
ARE THERE TWO OR MORE MASS IONS IN THE HIGH SENSITIVITY SET & HIGH SPECIFICITY SET?
YES
NO
D138
FINALLY SELECT BIOMARKER GROUP BY COMBINING CK NUMBER OF BIOMARKER GROUPS FROM AMONG THE BIOMARKER GROUPS
D139
DECIDE MASS IONS OF THE FINAL BIOMARKER GROUP AS LOW-MASS IONS FOR CRC SCREENING
END

FIG. 22

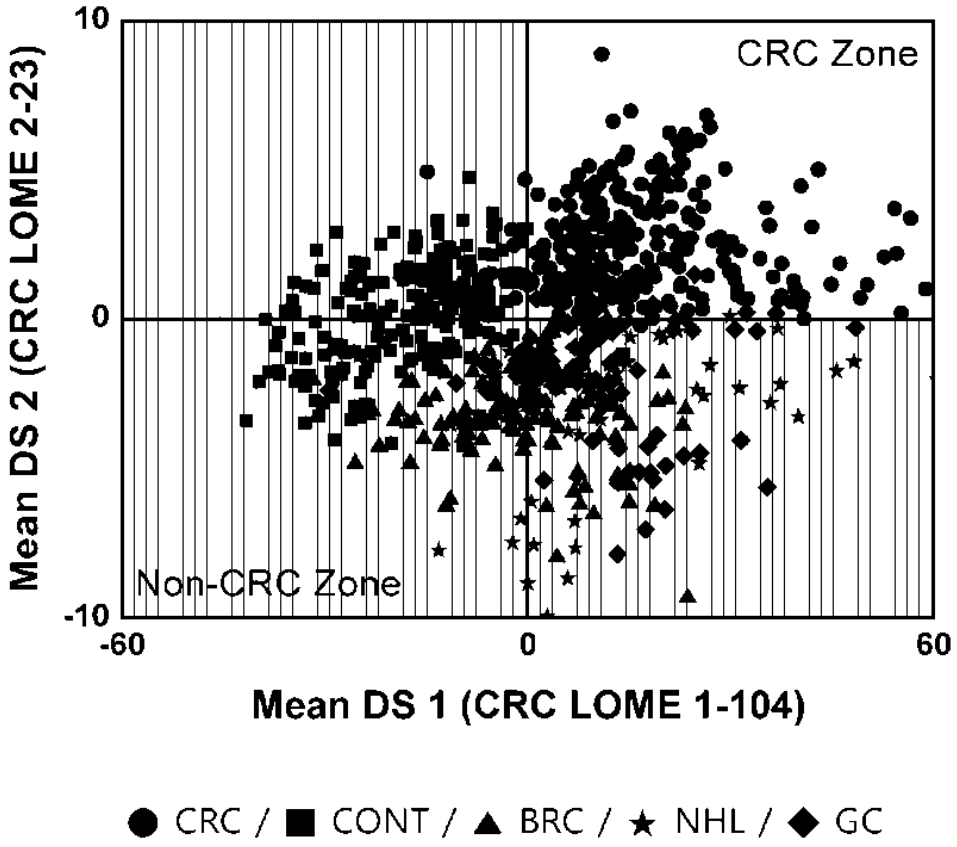

10
0
-10
-60
0
60
CRC Zone
Non-CRC Zone
Mean DS 2 (CRC LOME 2-23)
Mean DS 1 (CRC LOME 1-104)
● CRC / ■ CONT / ▲ BRC / ★ NHL / ◆ GC

FIG. 23

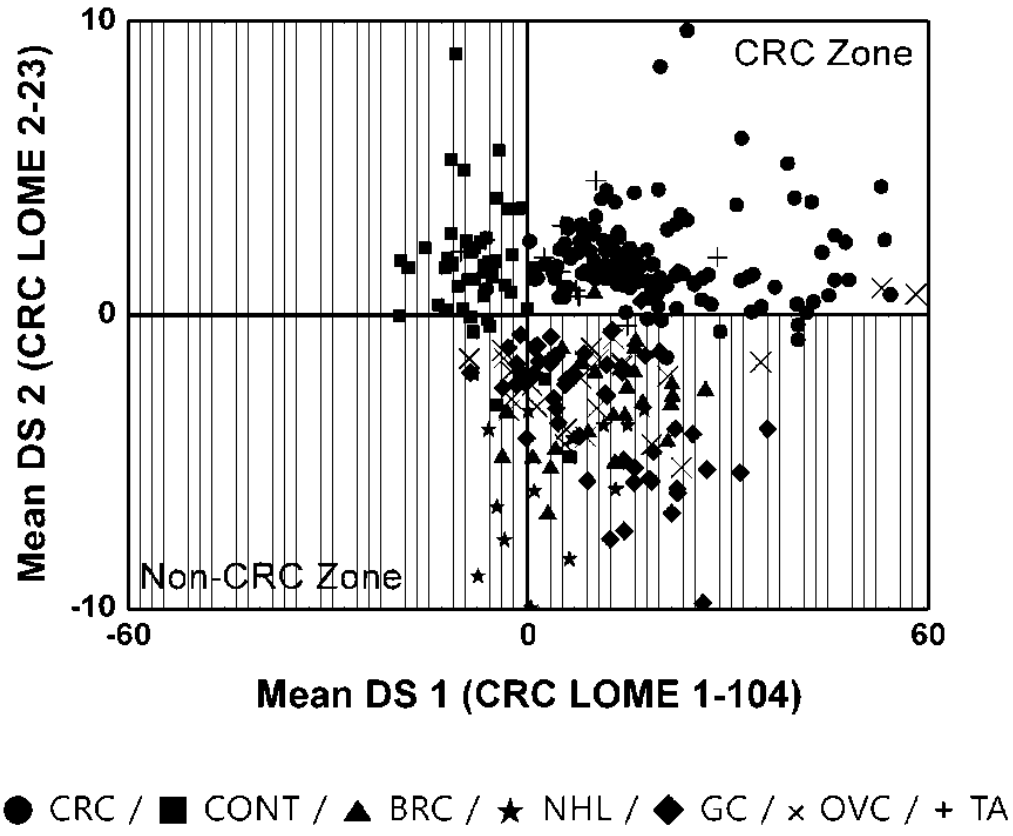
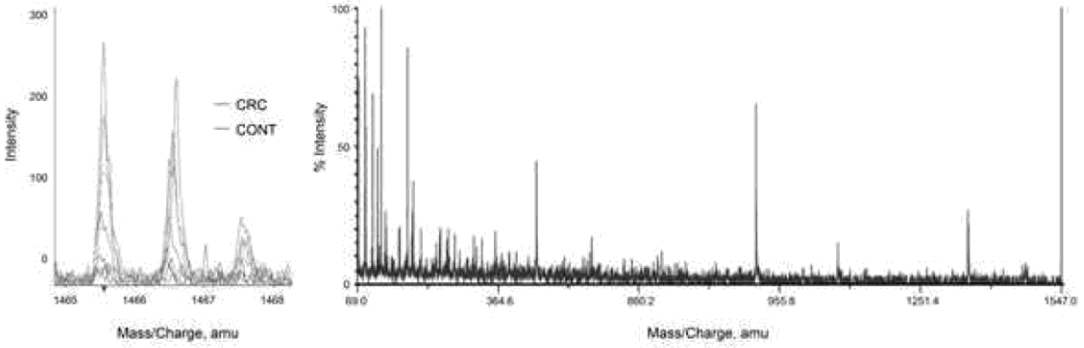

10
0
-10
-60
0
60
CRC Zone
Non-CRC Zone
Mean DS 2 (CRC LOME 2-23)
Mean DS 1 (CRC LOME 1-104)
● CRC / ■ CONT / ▲ BRC / ★ NHL / ◆ GC / × OVC / + TA

FIG. 24



Protein Name	Accession Number	Calc. Mass	Obsrv. Mass	Start Seq.	End Seq.	Sequence	Ion Score
Fibrinogen Alpha Chain	P02671	1464.6480	1465.7649	21	35	DSGEGDFLAEGGGVR	59

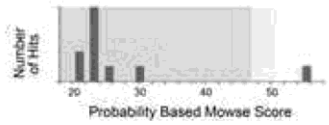
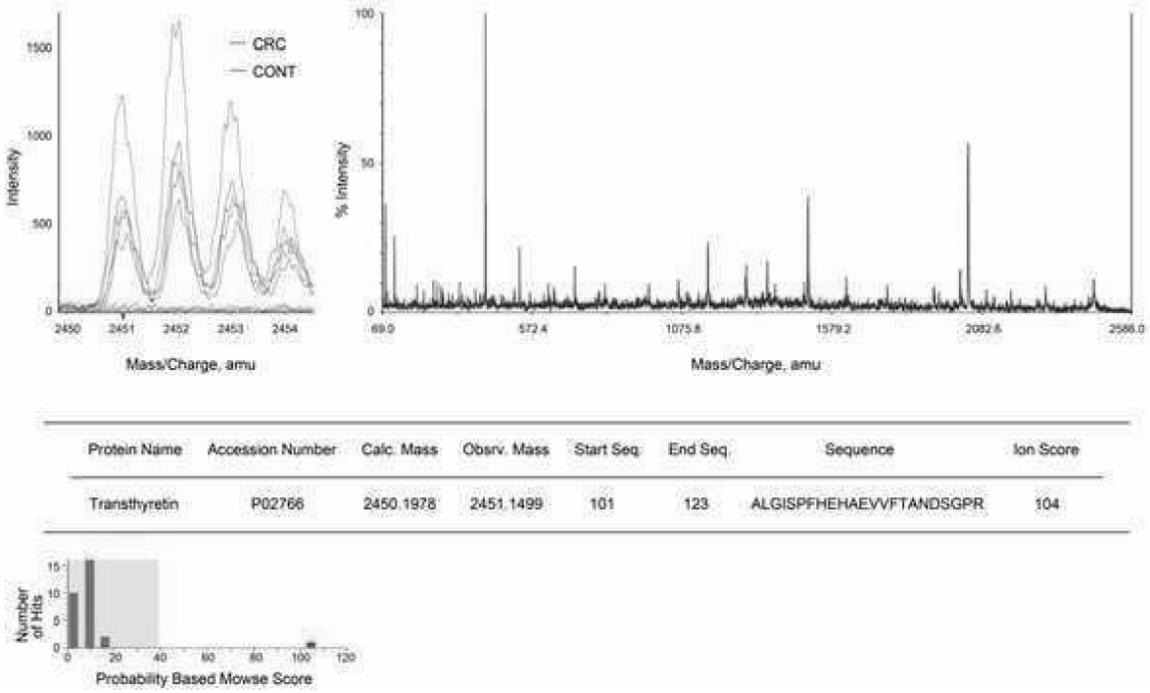


FIG. 25a



Protein Name	Accession Number	Calc. Mass	Obsrv. Mass	Start Seq.	End Seq.	Sequence	Ion Score
Transthyretin	P02766	2450.1978	2451.1499	101	123	ALGISPFHEHAEVVFTANDSGPR	104

FIG. 25b

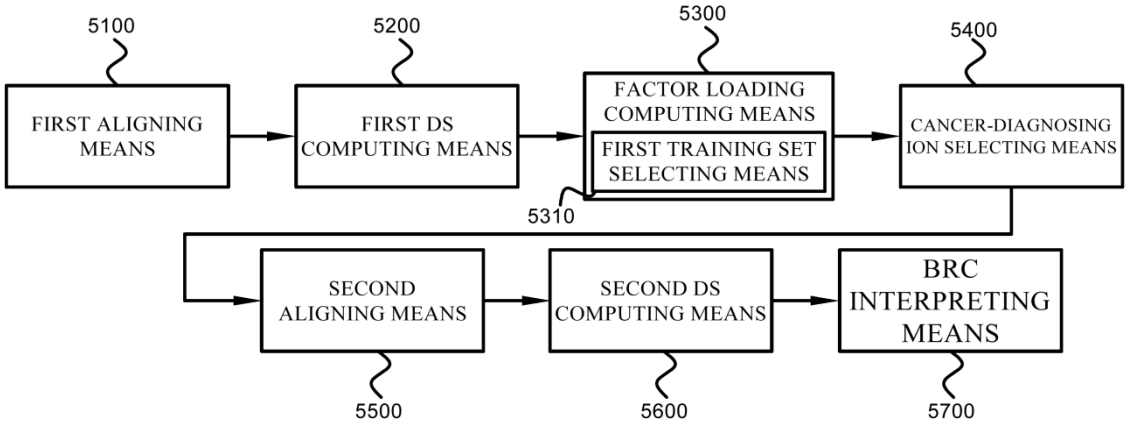

5100
FIRST ALIGNING MEANS
5200
FIRST DS COMPUTING MEANS
5300
FACTOR LOADING COMPUTING MEANS
FIRST TRAINING SET SELECTING MEANS
5310
5400
CANCER-DIAGNOSING ION SELECTING MEANS
SECOND ALIGNING MEANS
5500
SECOND DS COMPUTING MEANS
5600
BRC INTERPRETING MEANS
5700

FIG. 26

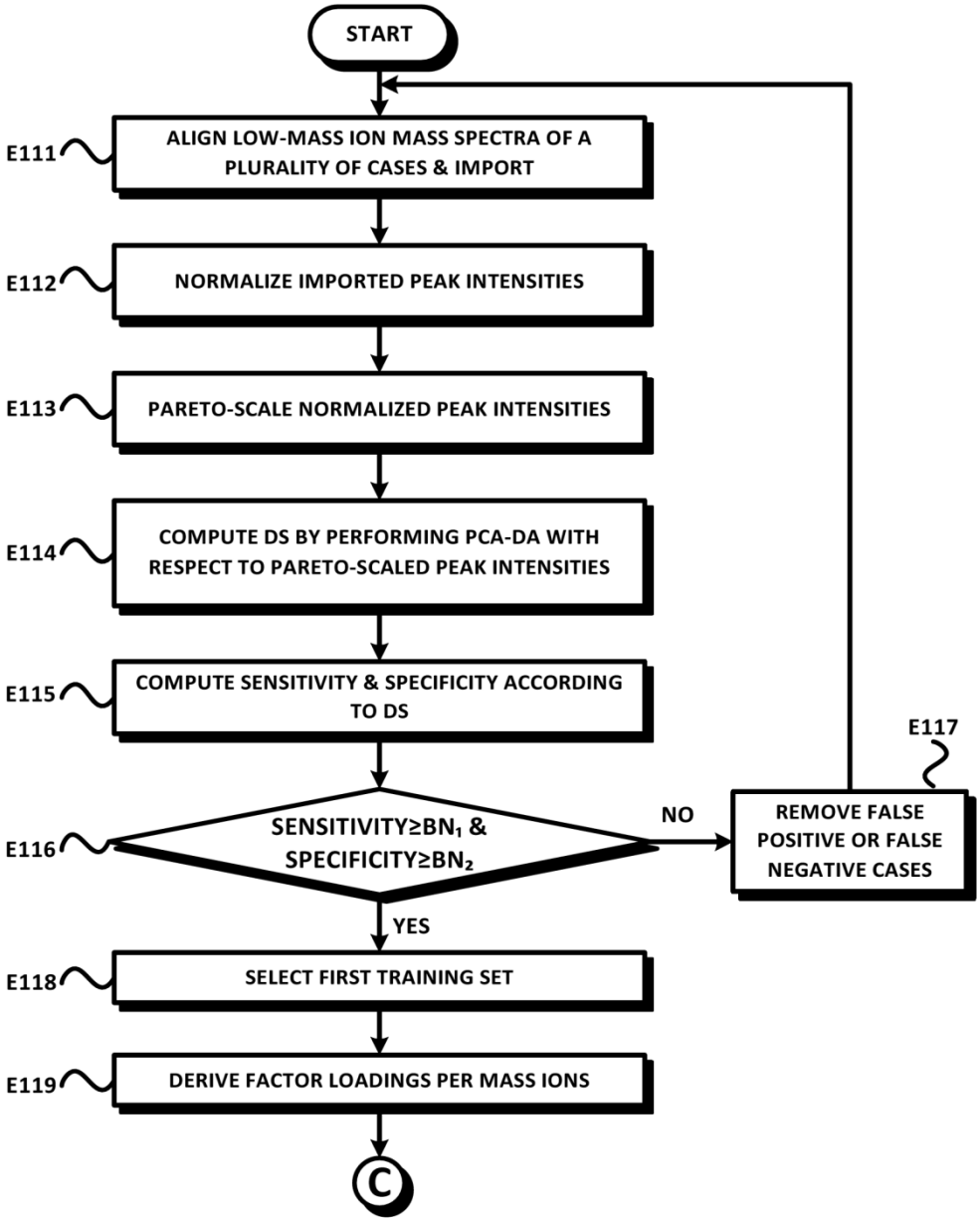

START
E111
ALIGN LOW-MASS ION MASS SPECTRA OF A PLURALITY OF CASES & IMPORT
E112
NORMALIZE IMPORTED PEAK INTENSITIES
E113
PARETO-SCALE NORMALIZED PEAK INTENSITIES
E114
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
E115
COMPUTE SENSITIVITY & SPECIFICITY ACCORDING TO DS
E116
SENSITIVITY≥BN1 & SPECIFICITY≥BN2
NO
E117
REMOVE FALSE POSITIVE OR FALSE NEGATIVE CASES
YES
E118
SELECT FIRST TRAINING SET
E119
DERIVE FACTOR LOADINGS PER MASS IONS
C

FIG 27

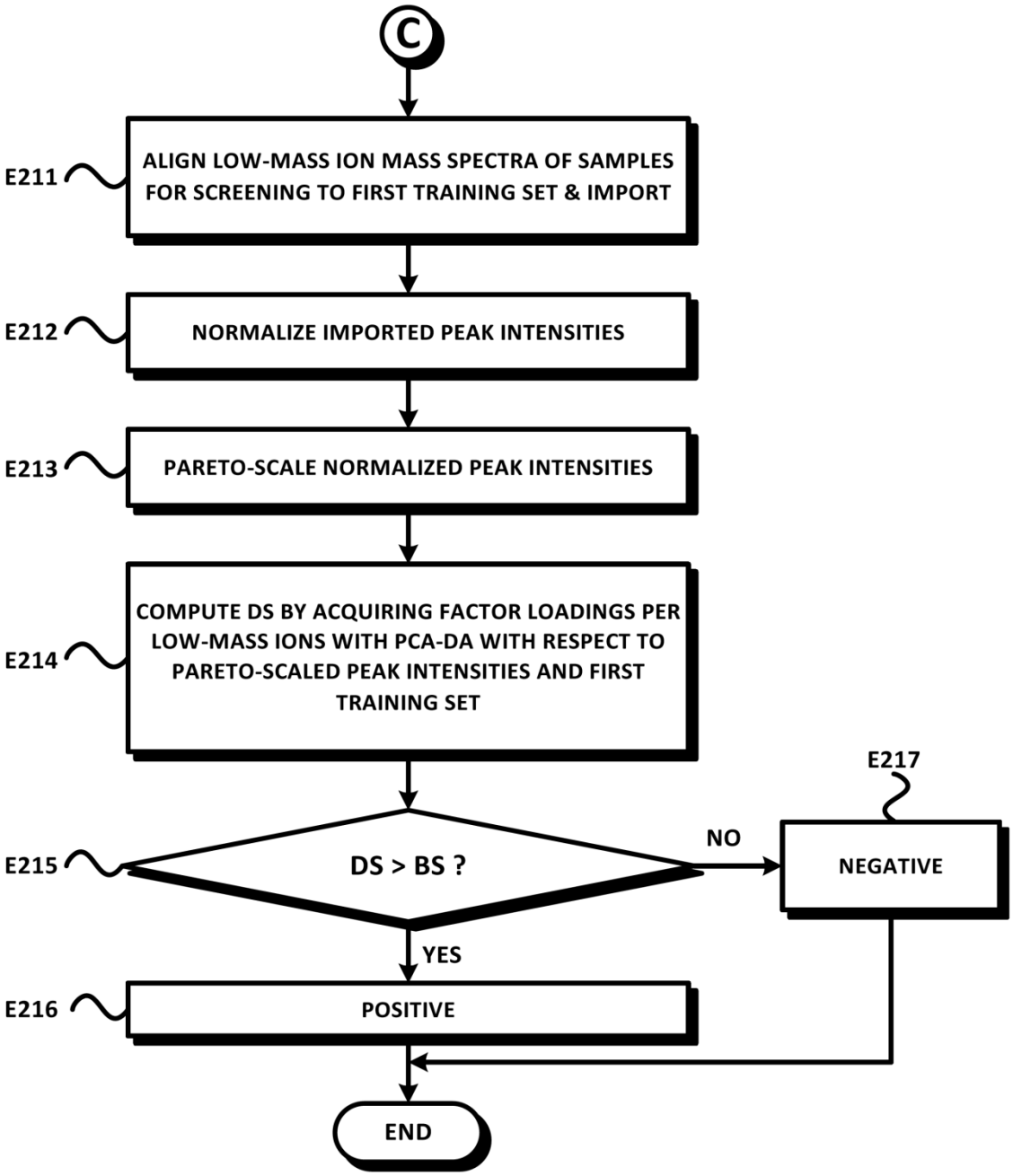

C
E211
ALIGN LOW-MASS ION MASS SPECTRA OF SAMPLES FOR SCREENING TO FIRST TRAINING SET & IMPORT
E212
NORMALIZE IMPORTED PEAK INTENSITIES
E213
PARETO-SCALE NORMALIZED PEAK INTENSITIES
E214
COMPUTE DS BY ACQUIRING FACTOR LOADINGS PER LOW-MASS IONS WITH PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES AND FIRST TRAINING SET
E215
DS > BS ?
NO
E217
NEGATIVE
YES
E216
POSITIVE
END

FIG 28

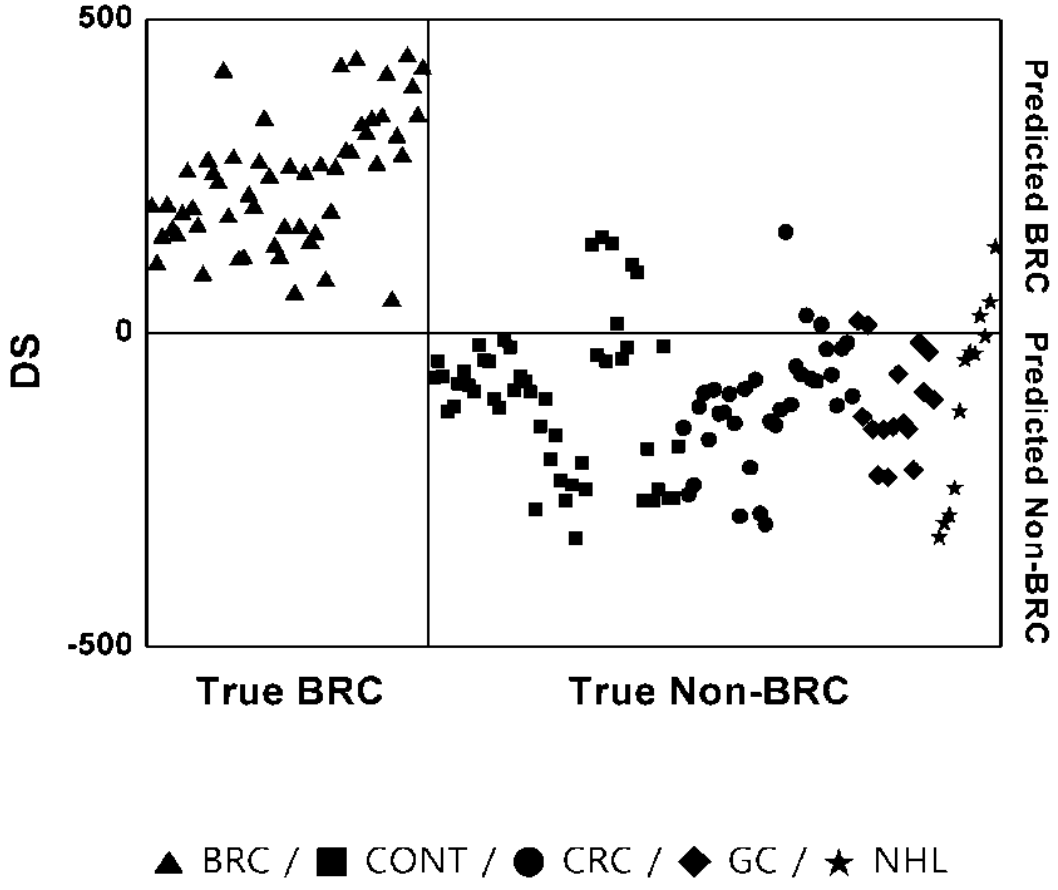
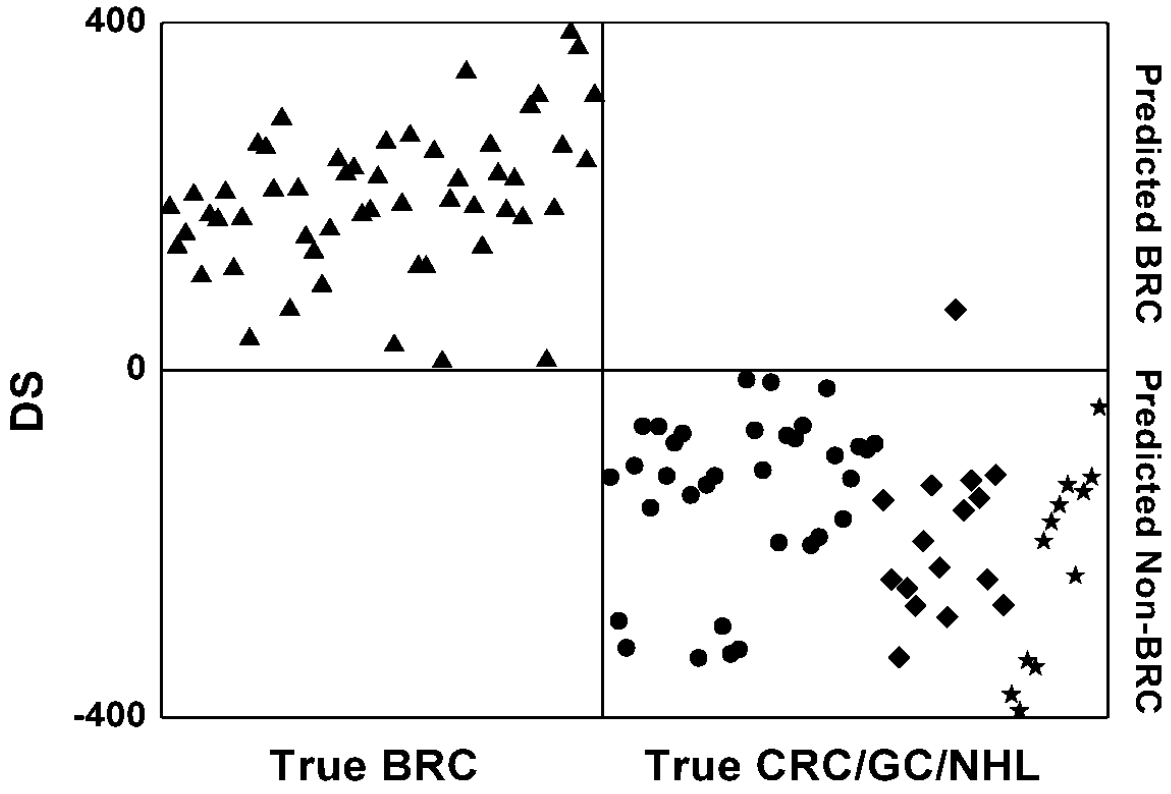

500
0
-500
DS
True BRC
True Non-BRC
Predicted BRC
Predicted Non-BRC
▲ BRC / ■ CONT / ● CRC / ◆ GC / ★ NHL

FIG 29



▲ BRC / ● CRC / ◆ GC / ★ NHL

FIG. 30

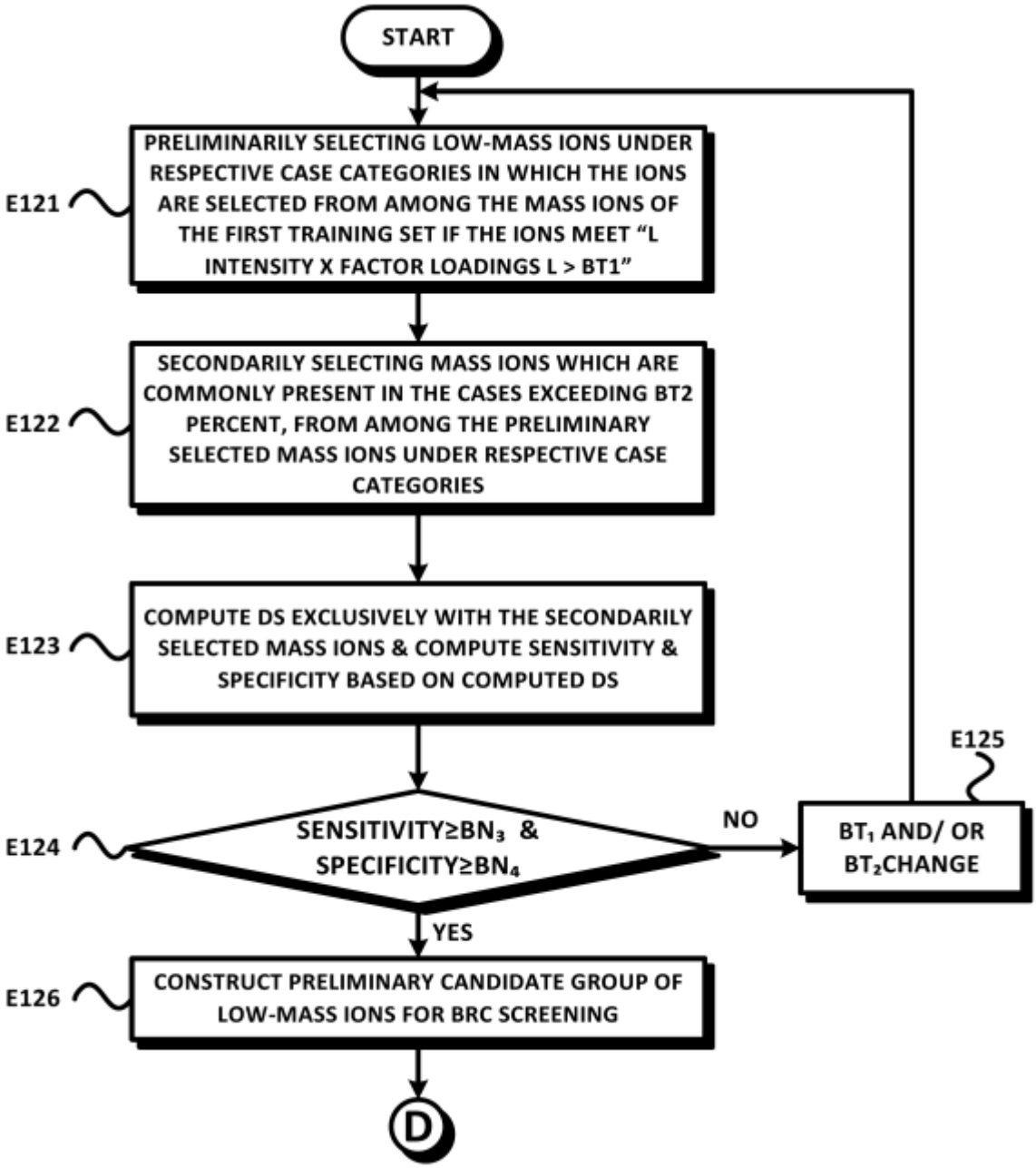

START
PRELIMINARILY SELECTING LOW-MASS IONS UNDER RESPECTIVE CASE CATEGORIES IN WHICH THE IONS ARE SELECTED FROM AMONG THE MASS IONS OF THE FIRST TRAINING SET IF THE IONS MEET "L INTENSITY X FACTOR LOADINGS L > BT1"
E121
SECONDARILY SELECTING MASS IONS WHICH ARE COMMONLY PRESENT IN THE CASES EXCEEDING BT2 PERCENT, FROM AMONG THE PRELIMINARY SELECTED MASS IONS UNDER RESPECTIVE CASE CATEGORIES
E122
COMPUTE DS EXCLUSIVELY WITH THE SECONDARILY SELECTED MASS IONS & COMPUTE SENSITIVITY & SPECIFICITY BASED ON COMPUTED DS
E123
SENSITIVITY≥BN3 & SPECIFICITY≥BN4
E124
NO
BT1 AND/ OR BT2CHANGE
E125
YES
CONSTRUCT PRELIMINARY CANDIDATE GROUP OF LOW-MASS IONS FOR BRC SCREENING
E126
D

FIG. 31

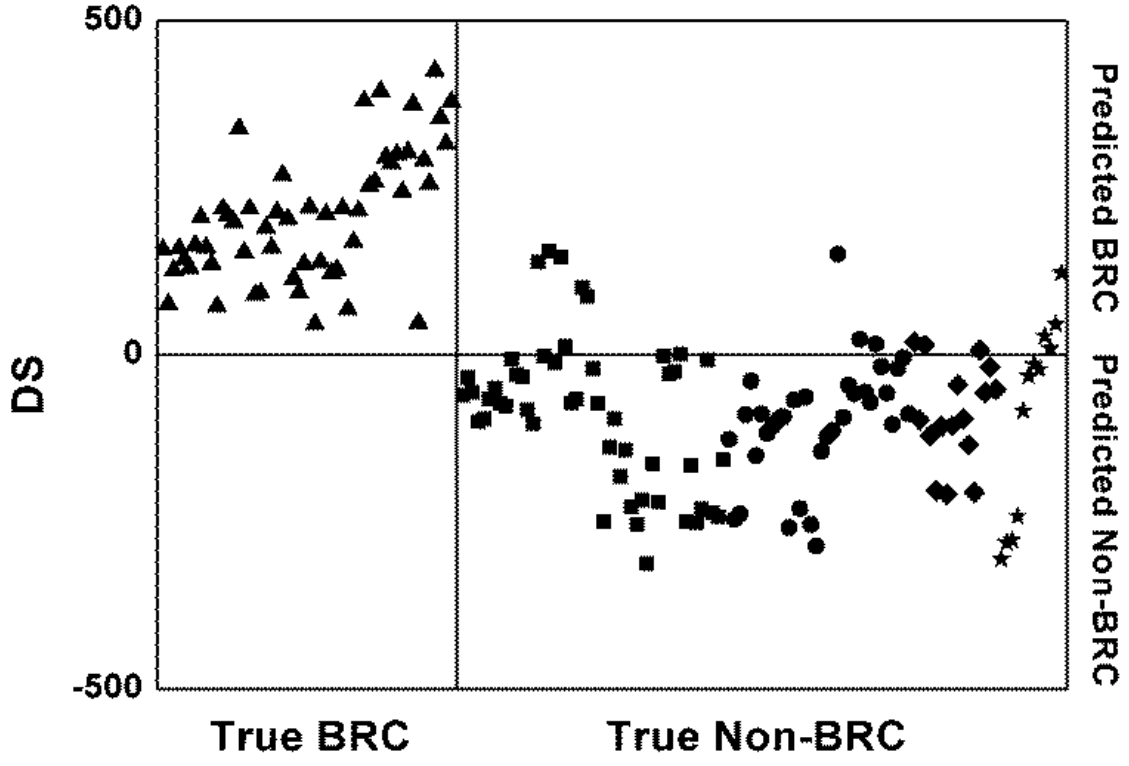
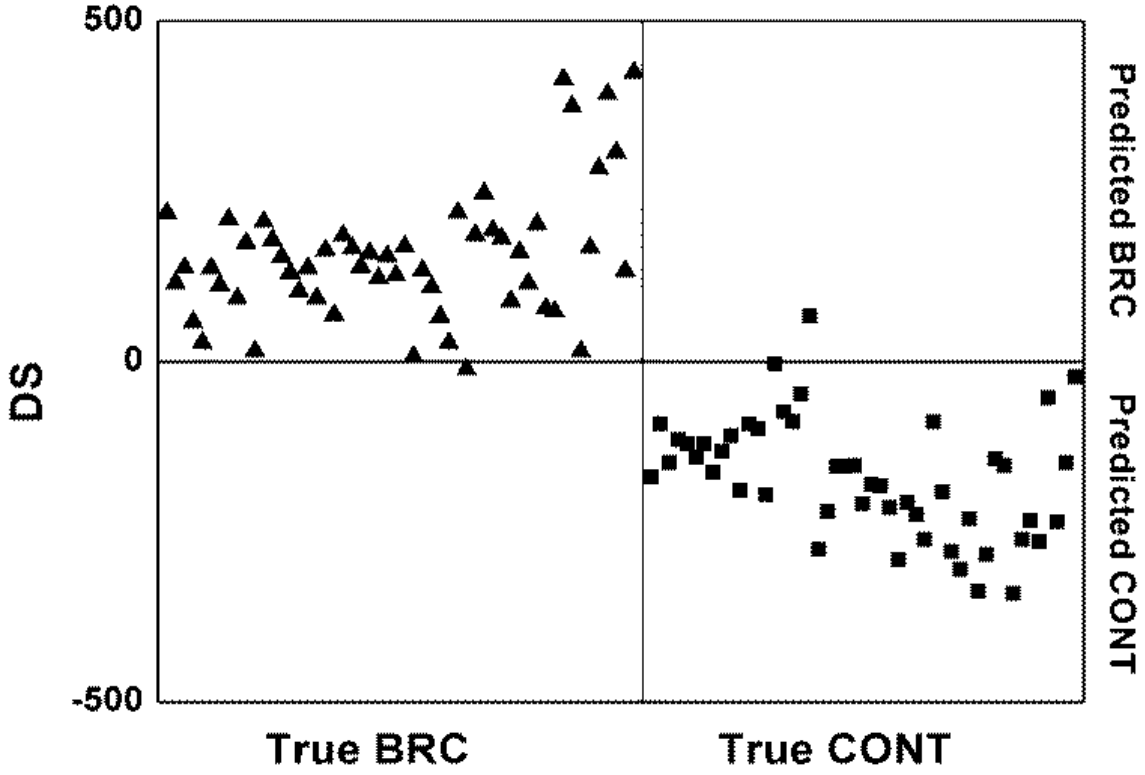

500
0
-500
DS
True BRC
True Non-BRC
Predicted BRC
Predicted Non-BRC
▲ BRC / ■ CONT / ● CRC / ◆ GC / ★ NHL

FIG. 32



▲ BRC / ■ CONT

FIG. 33

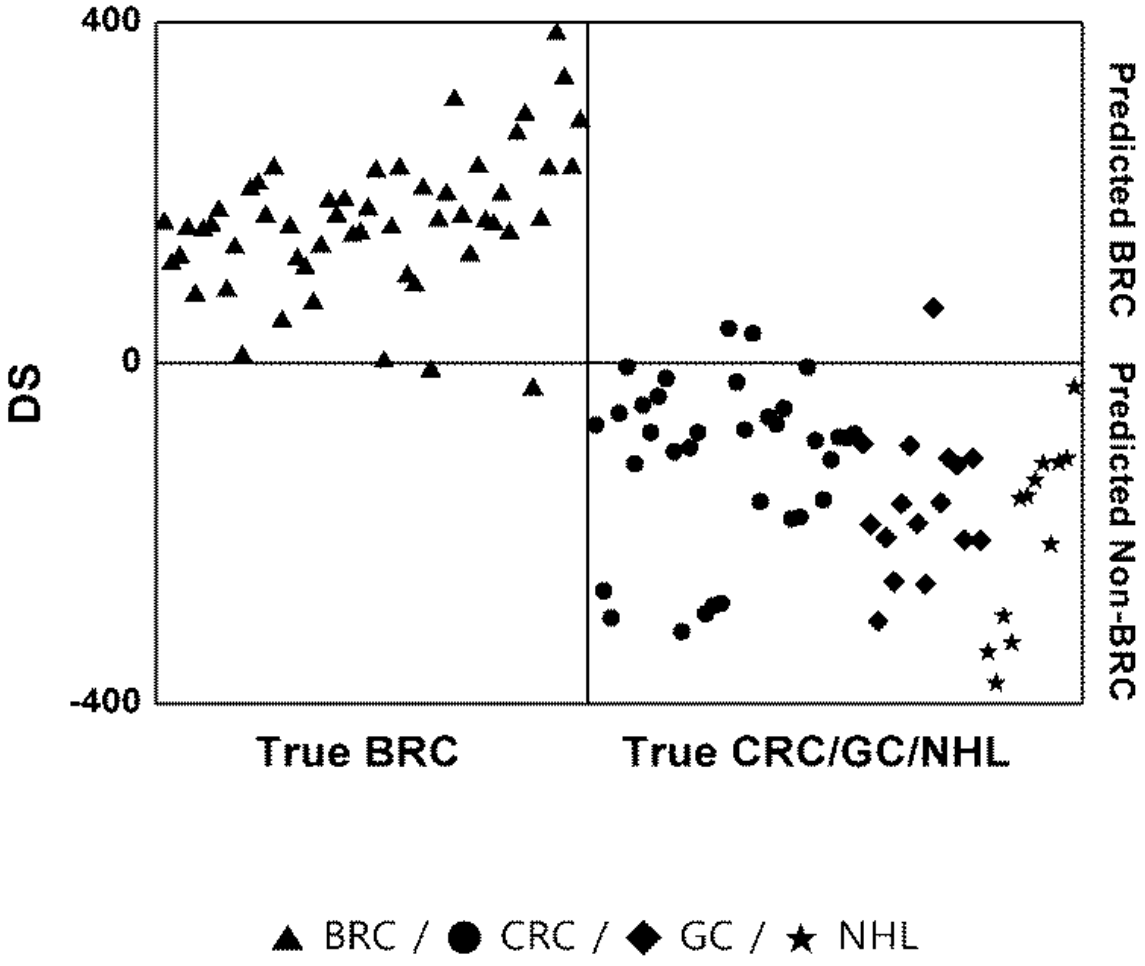

400
0
-400
DS
Predicted BRC
Predicted Non-BRC
True BRC
True CRC/GC/NHL
▲ BRC / ● CRC / ◆ GC / ★ NHL

FIG. 34

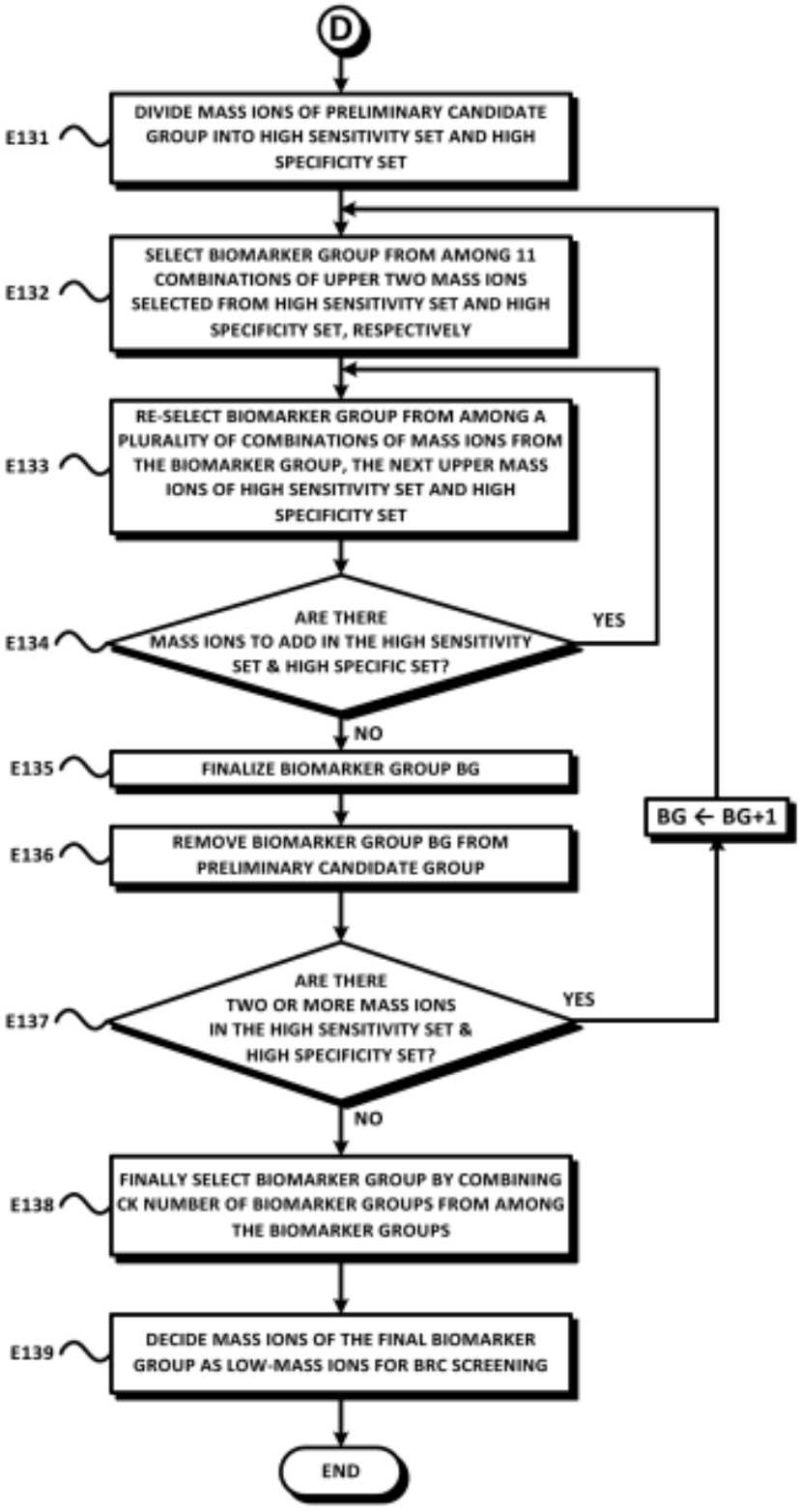
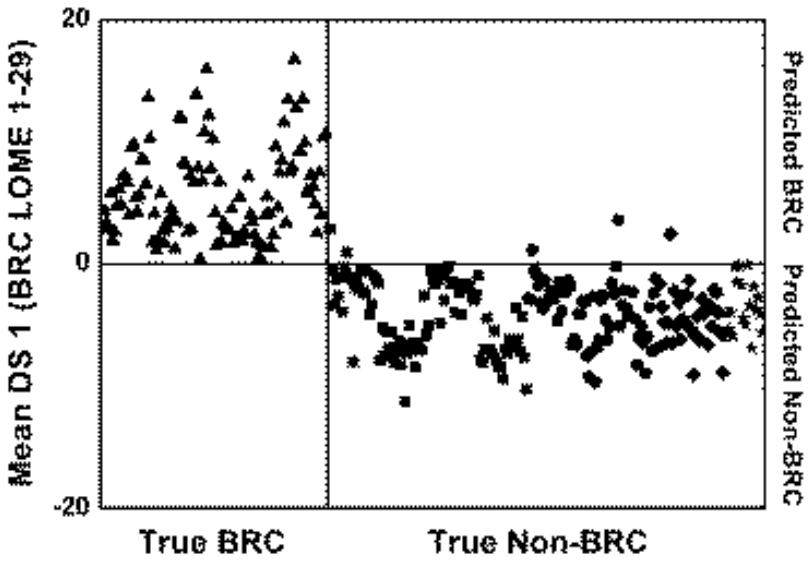

D
E131
DIVIDE MASS IONS OF PRELIMINARY CANDIDATE GROUP INTO HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
E132
SELECT BIOMARKER GROUP FROM AMONG 11 COMBINATIONS OF UPPER TWO MASS IONS SELECTED FROM HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET, RESPECTIVELY
E133
RE-SELECT BIOMARKER GROUP FROM AMONG A PLURALITY OF COMBINATIONS OF MASS IONS FROM THE BIOMARKER GROUP, THE NEXT UPPER MASS IONS OF HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
E134
ARE THERE MASS IONS TO ADD IN THE HIGH SENSITIVITY SET & HIGH SPECIFIC SET?
YES
NO
E135
FINALIZE BIOMARKER GROUP BG
E136
REMOVE BIOMARKER GROUP BG FROM PRELIMINARY CANDIDATE GROUP
BG ← BG+1
E137
ARE THERE TWO OR MORE MASS IONS IN THE HIGH SENSITIVITY SET & HIGH SPECIFICITY SET?
YES
NO
E138
FINALLY SELECT BIOMARKER GROUP BY COMBINING CK NUMBER OF BIOMARKER GROUPS FROM AMONG THE BIOMARKER GROUPS
E139
DECIDE MASS IONS OF THE FINAL BIOMARKER GROUP AS LOW-MASS IONS FOR BRC SCREENING
END

FIG. 35


20
0
-20
Mean DS 1 (BRC LOME 1-29)
Predicted BRC
Predicted Non-BRC
True BRC
True Non-BRC

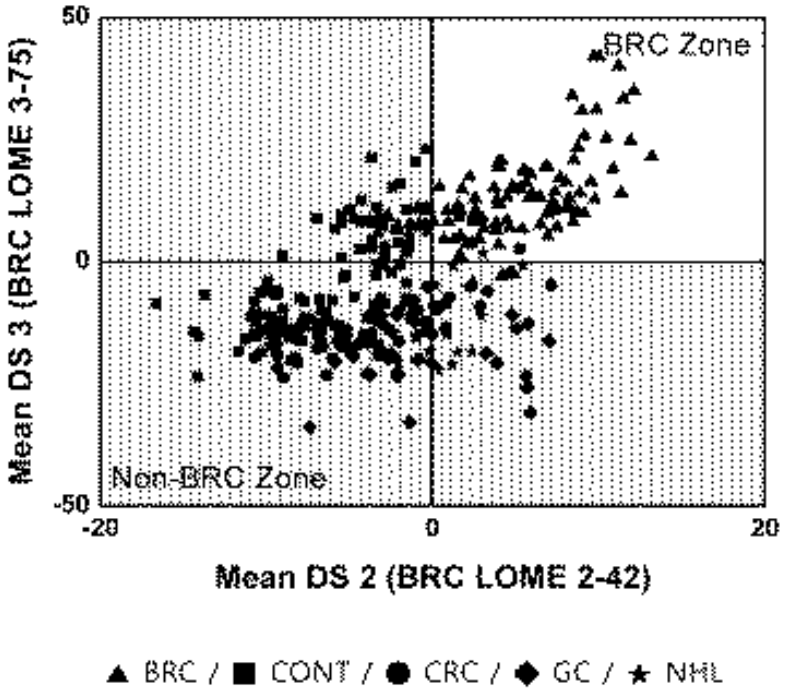
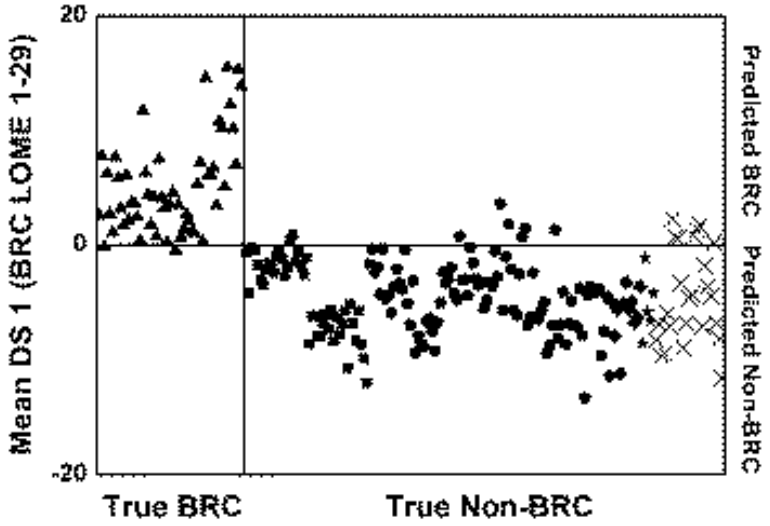
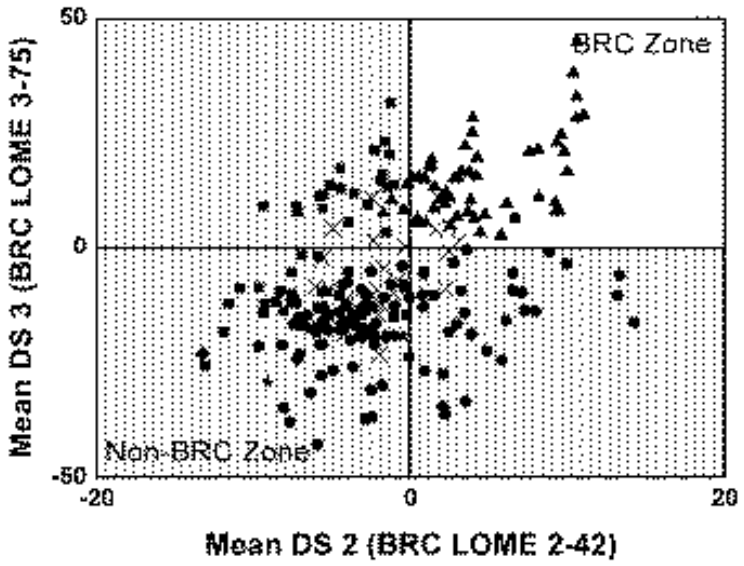

50
0
-50
-20
0
20
Mean DS 3 (BRC LOME 3-75)
Mean DS 2 (BRC LOME 2-42)
BRC Zone
Non-BRC Zone
▲ BRC / ■ CONT / ● CRC / ◆ GC / ★ NHL

FIG. 36





▲ BRC / ■ CONT / ● CRC / ◆ GC / ★ NHL / × OVC

FIG. 37

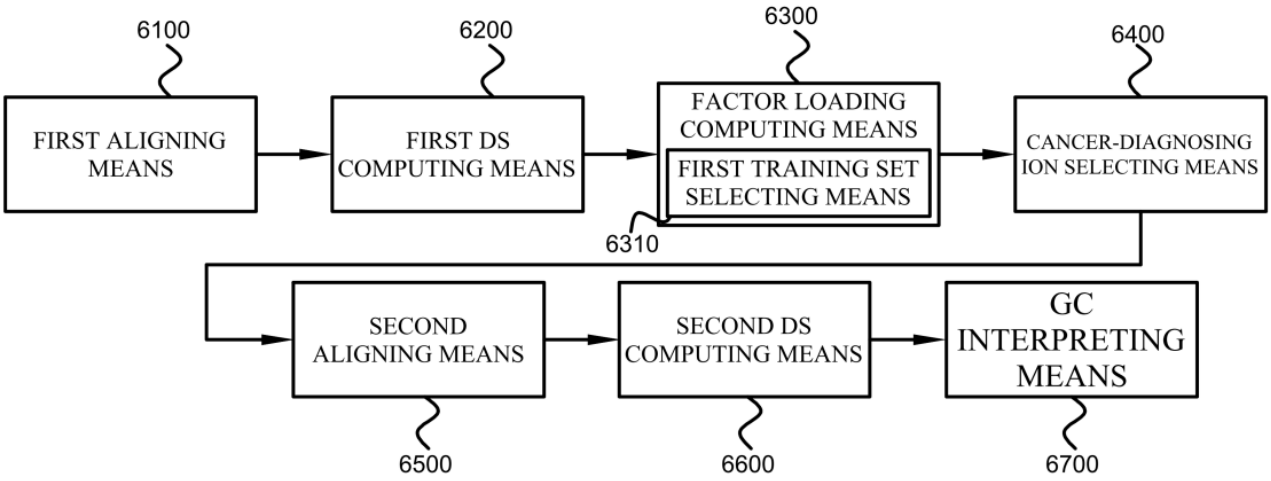

6100
FIRST ALIGNING MEANS
6200
FIRST DS COMPUTING MEANS
6300
FACTOR LOADING COMPUTING MEANS
FIRST TRAINING SET SELECTING MEANS
6310
6400
CANCER-DIAGNOSING ION SELECTING MEANS
SECOND ALIGNING MEANS
6500
SECOND DS COMPUTING MEANS
6600
GC INTERPRETING MEANS
6700

FIG. 38

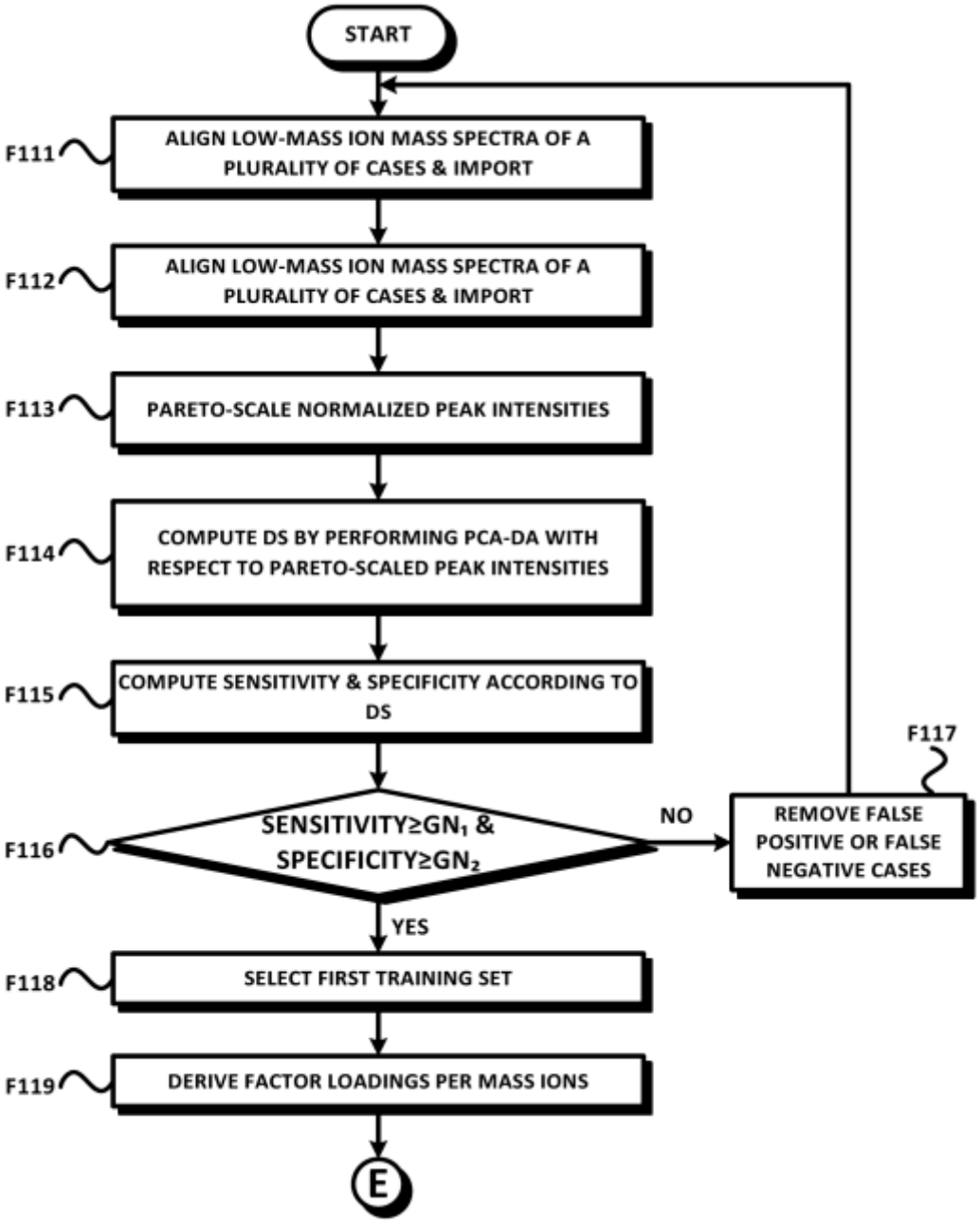

START
F111
ALIGN LOW-MASS ION MASS SPECTRA OF A PLURALITY OF CASES & IMPORT
F112
ALIGN LOW-MASS ION MASS SPECTRA OF A PLURALITY OF CASES & IMPORT
F113
PARETO-SCALE NORMALIZED PEAK INTENSITIES
F114
COMPUTE DS BY PERFORMING PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES
F115
COMPUTE SENSITIVITY & SPECIFICITY ACCORDING TO DS
F116
SENSITIVITY≥GN1 & SPECIFICITY≥GN2
NO
F117
REMOVE FALSE POSITIVE OR FALSE NEGATIVE CASES
YES
F118
SELECT FIRST TRAINING SET
F119
DERIVE FACTOR LOADINGS PER MASS IONS
E

FIG. 39

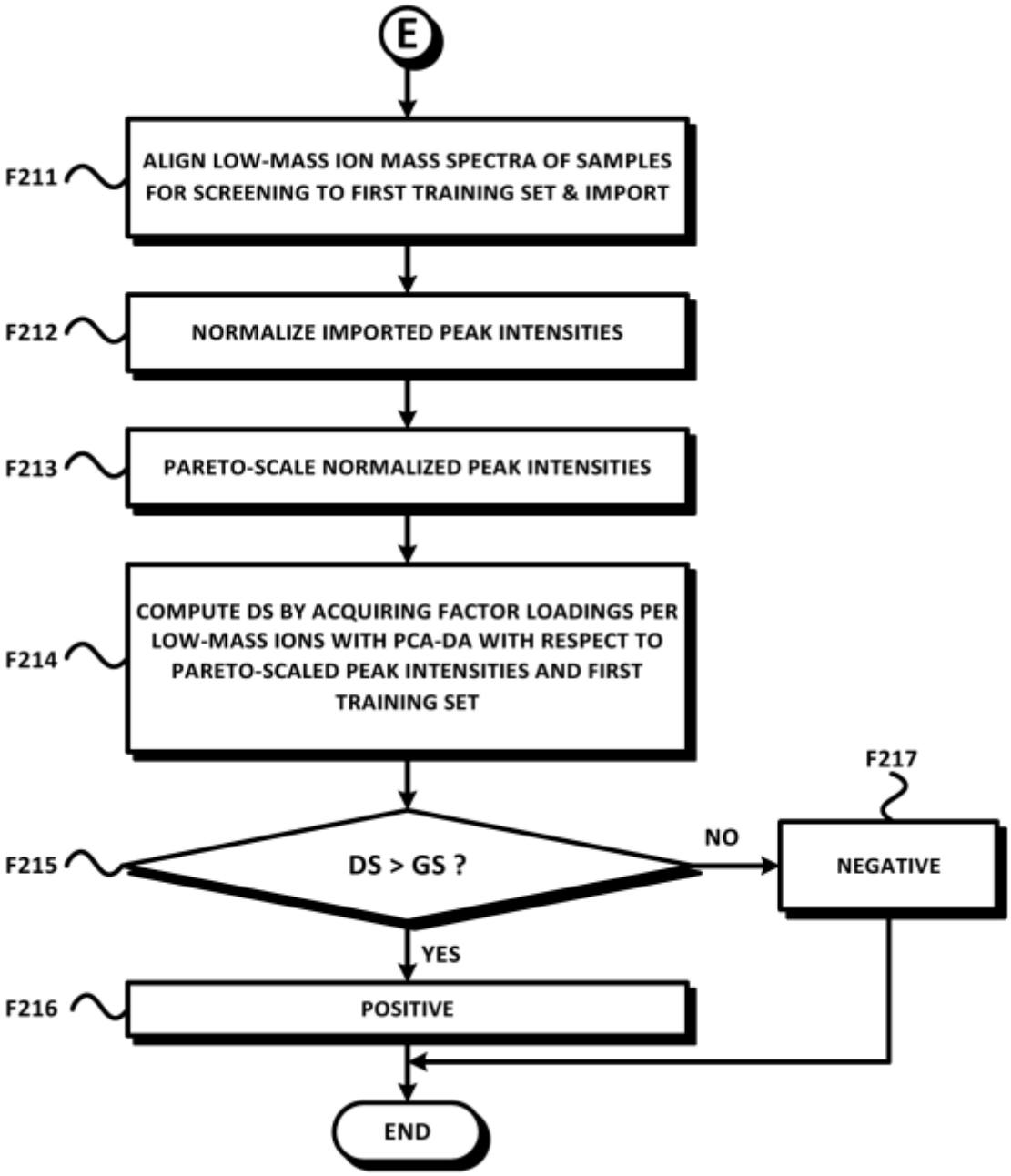
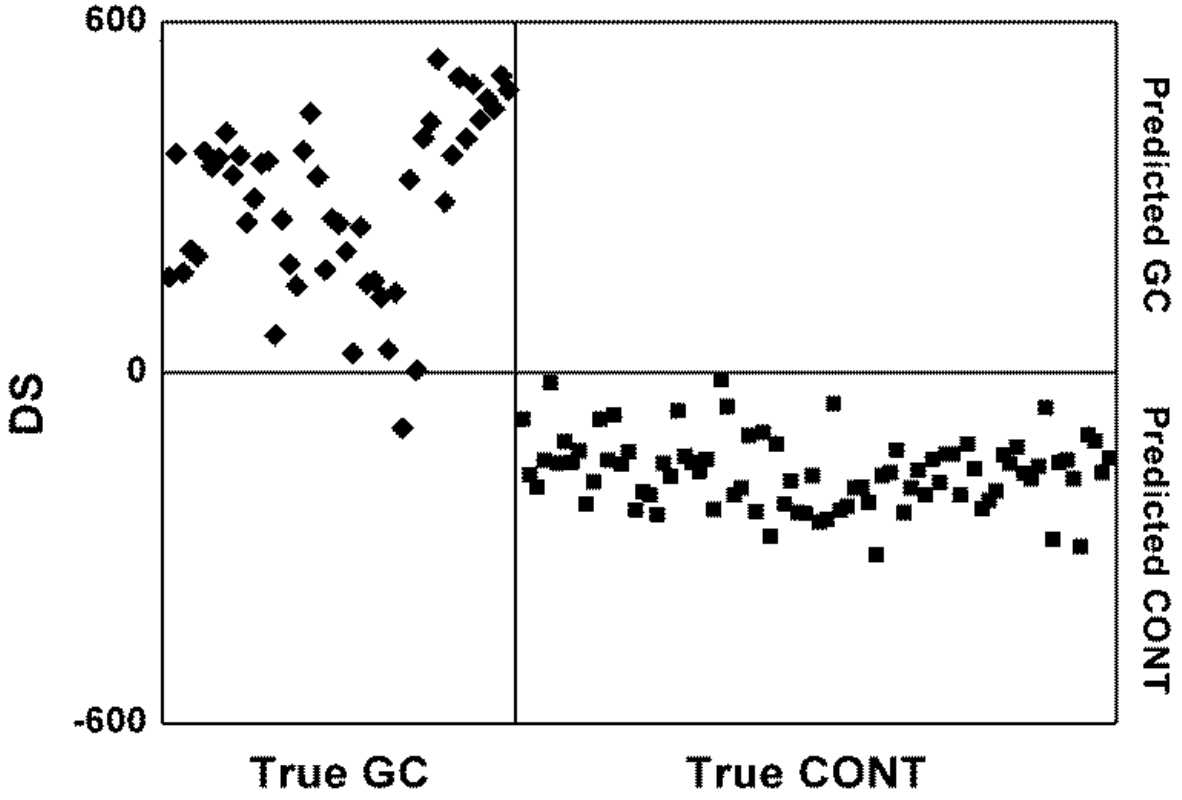
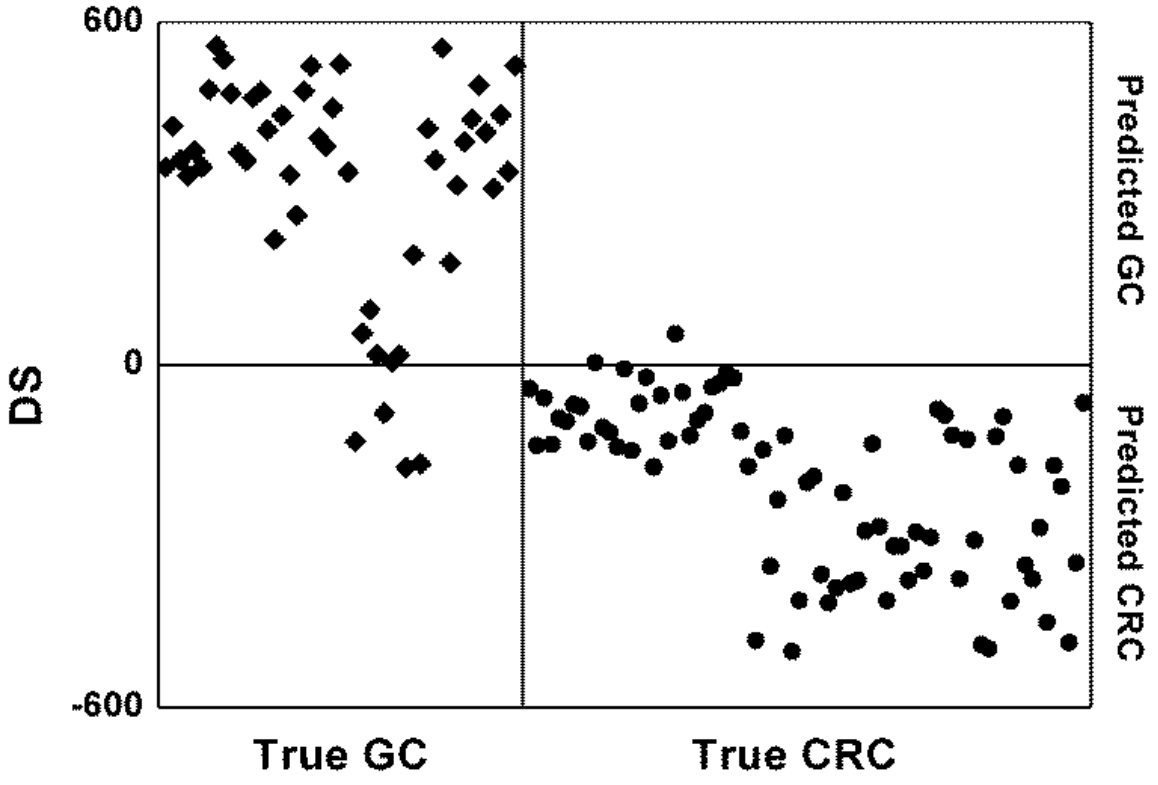

E
F211
ALIGN LOW-MASS ION MASS SPECTRA OF SAMPLES FOR SCREENING TO FIRST TRAINING SET & IMPORT
F212
NORMALIZE IMPORTED PEAK INTENSITIES
F213
PARETO-SCALE NORMALIZED PEAK INTENSITIES
F214
COMPUTE DS BY ACQUIRING FACTOR LOADINGS PER LOW-MASS IONS WITH PCA-DA WITH RESPECT TO PARETO-SCALED PEAK INTENSITIES AND FIRST TRAINING SET
F215
DS > GS ?
NO
F217
NEGATIVE
YES
F216
POSITIVE
END

FIG. 40



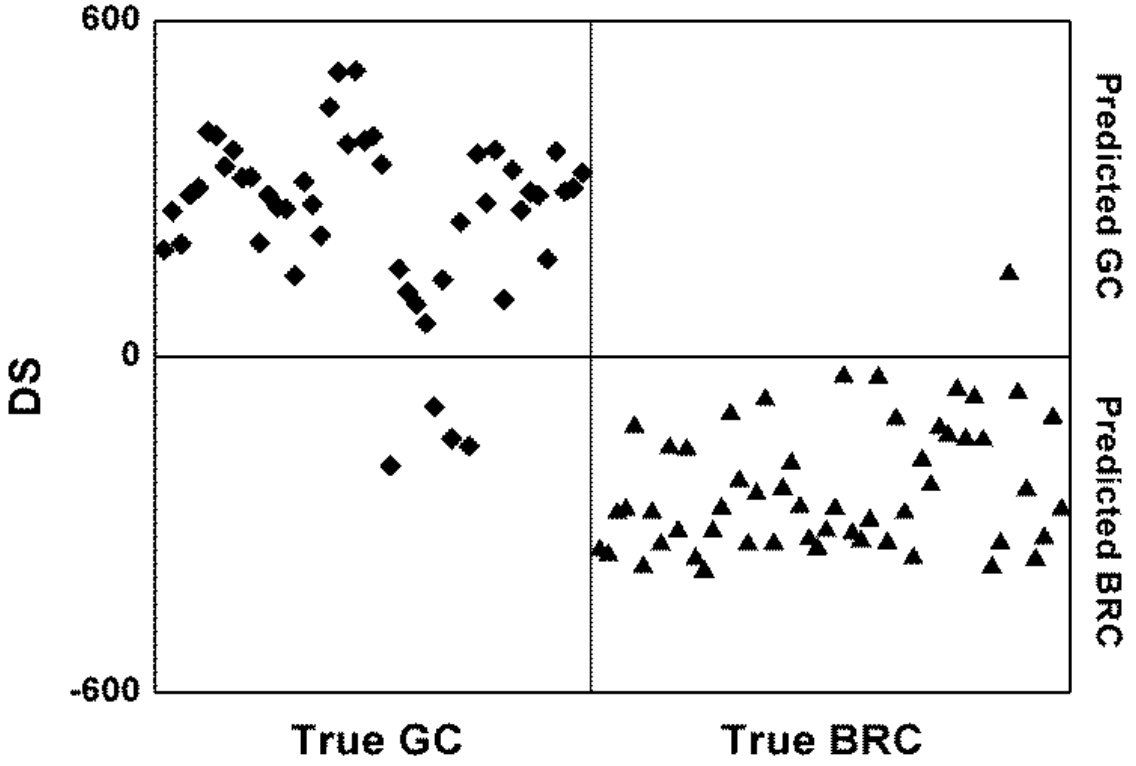
◆ GC / ■ CONT

FIG. 41



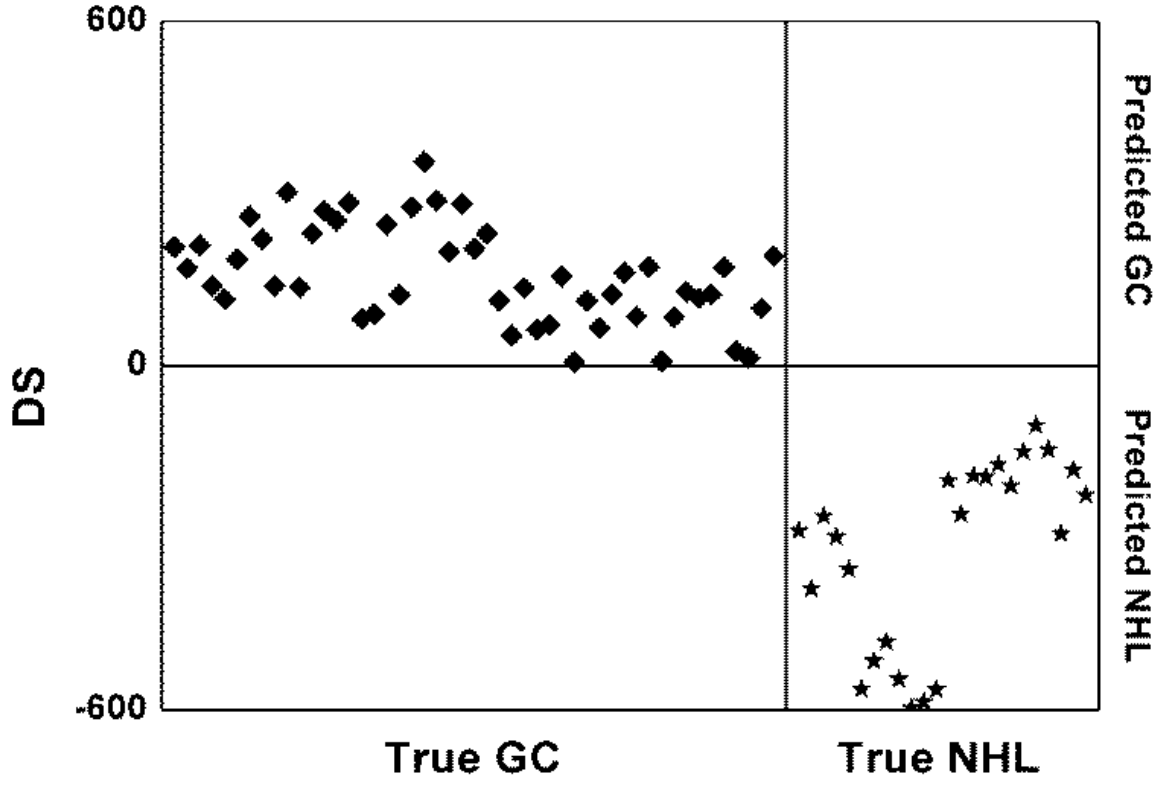
◆ GC / ● CRC

FIG. 42



◆ GC / ▲ BRC

FIG. 43



◆ GC / ★ NHL

FIG. 44

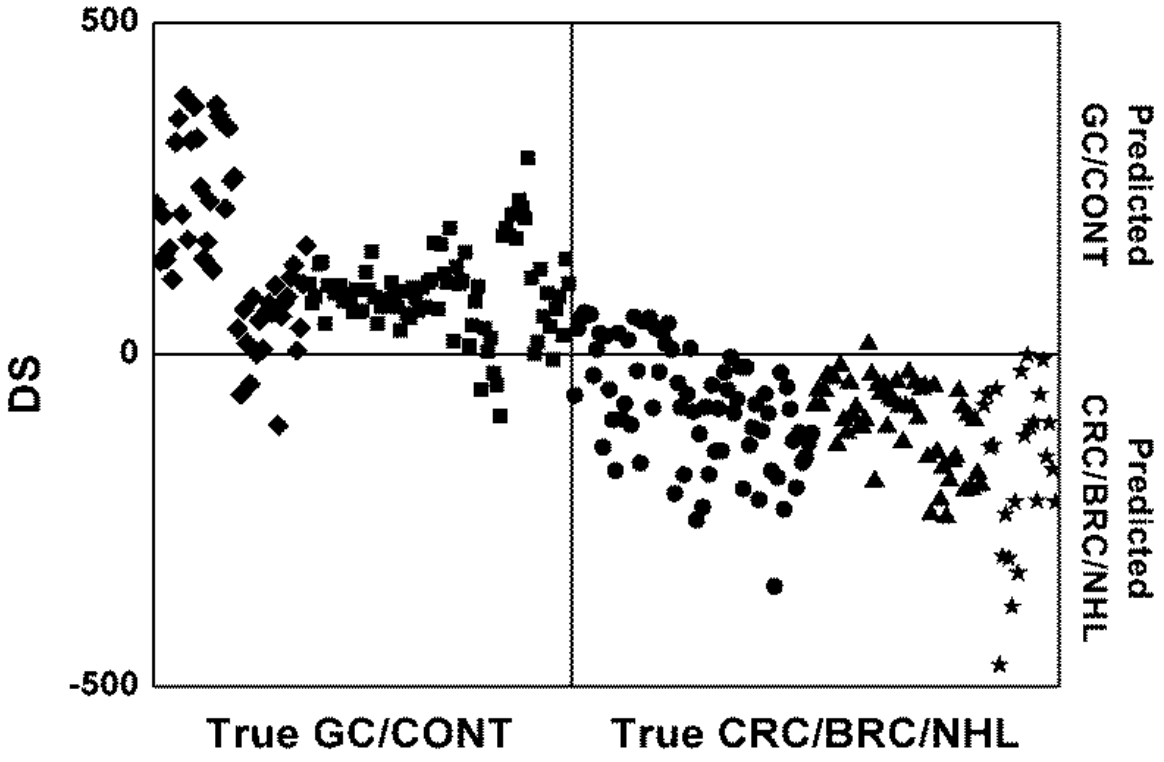

500
0
-500
DS
Predicted GC/CONT
Predicted CRC/BRC/NHL
True GC/CONT
True CRC/BRC/NHL
◆ GC / ■ CONT / ● CRC / ▲ BRC / ★ NHL

FIG. 45

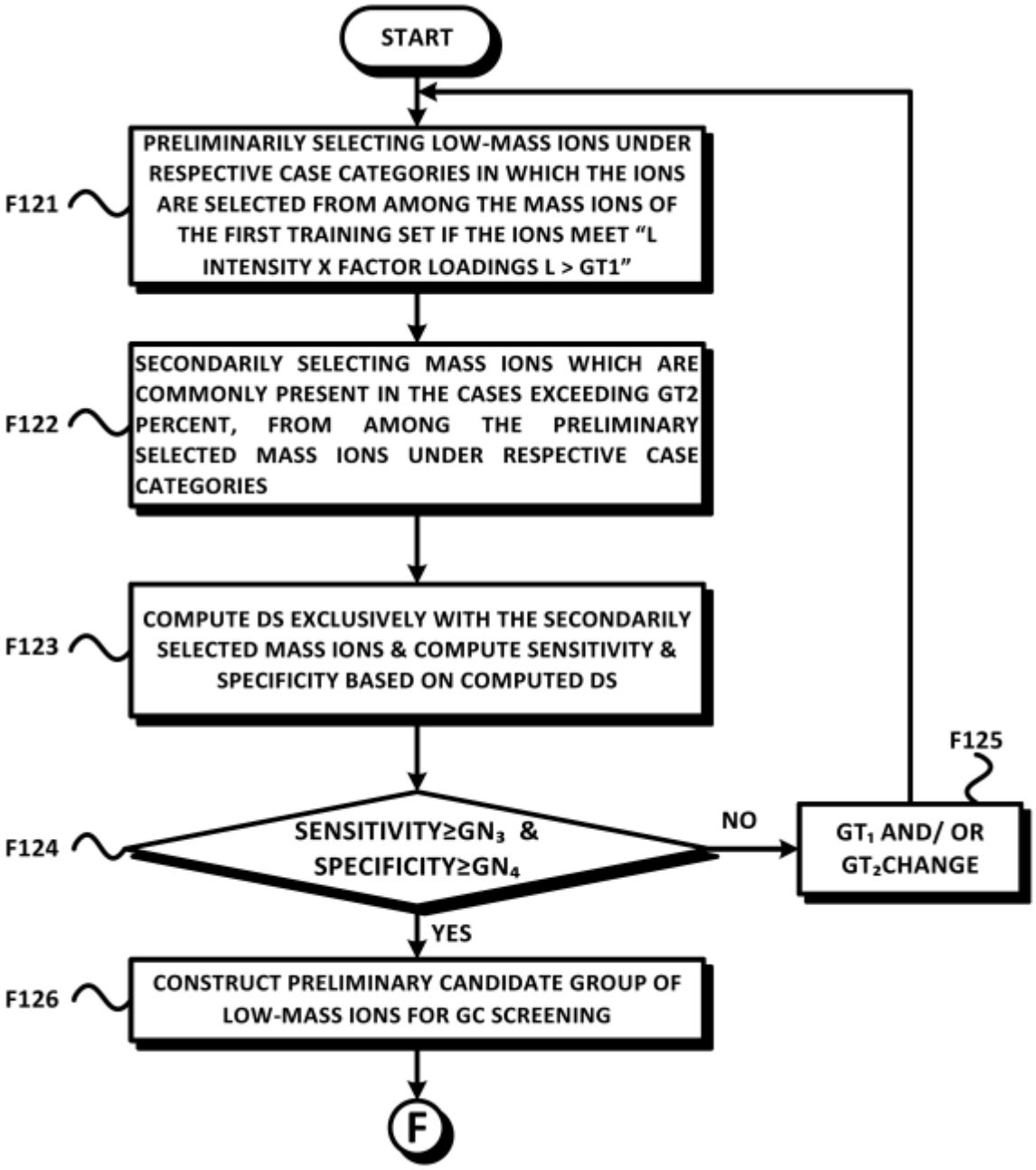
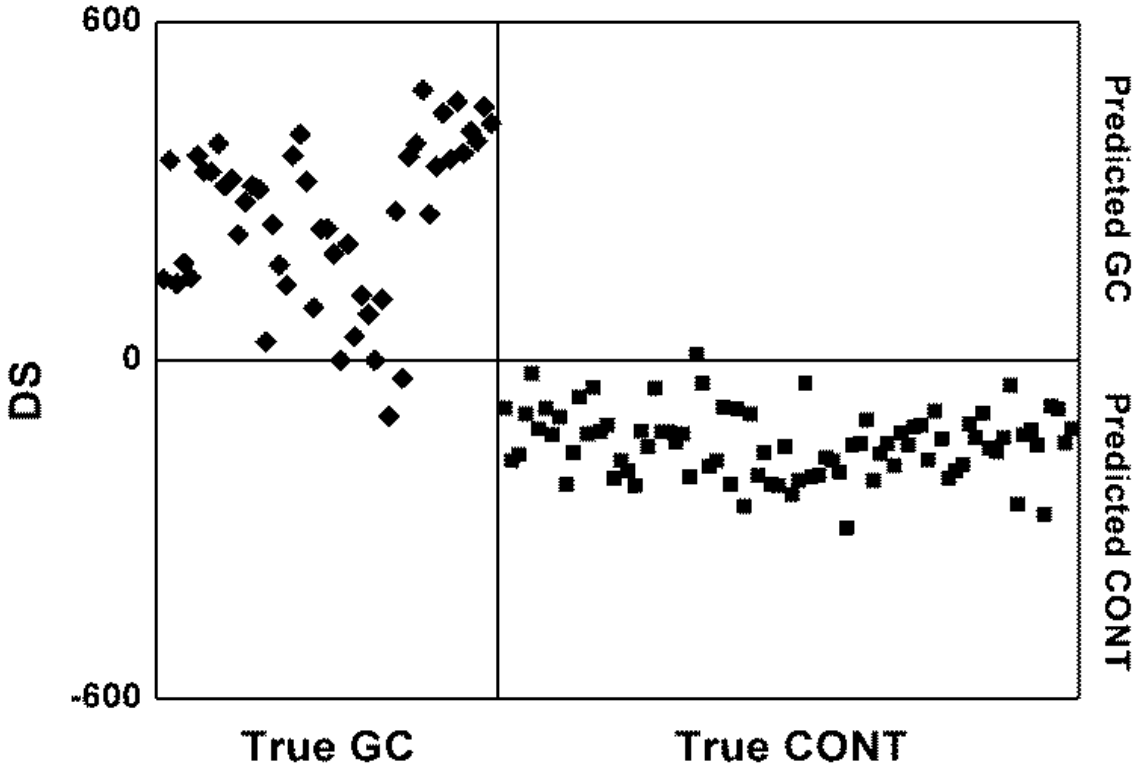

START
PRELIMINARILY SELECTING LOW-MASS IONS UNDER RESPECTIVE CASE CATEGORIES IN WHICH THE IONS ARE SELECTED FROM AMONG THE MASS IONS OF THE FIRST TRAINING SET IF THE IONS MEET "L INTENSITY X FACTOR LOADINGS L > GT1"
F121
SECONDARILY SELECTING MASS IONS WHICH ARE COMMONLY PRESENT IN THE CASES EXCEEDING GT2 PERCENT, FROM AMONG THE PRELIMINARY SELECTED MASS IONS UNDER RESPECTIVE CASE CATEGORIES
F122
COMPUTE DS EXCLUSIVELY WITH THE SECONDARILY SELECTED MASS IONS & COMPUTE SENSITIVITY & SPECIFICITY BASED ON COMPUTED DS
F123
SENSITIVITY≥GN3 & SPECIFICITY≥GN4
F124
NO
GT1 AND/ OR GT2CHANGE
F125
YES
CONSTRUCT PRELIMINARY CANDIDATE GROUP OF LOW-MASS IONS FOR GC SCREENING
F126
F

FIG. 46



◆ GC / ■ CONT

FIG. 47

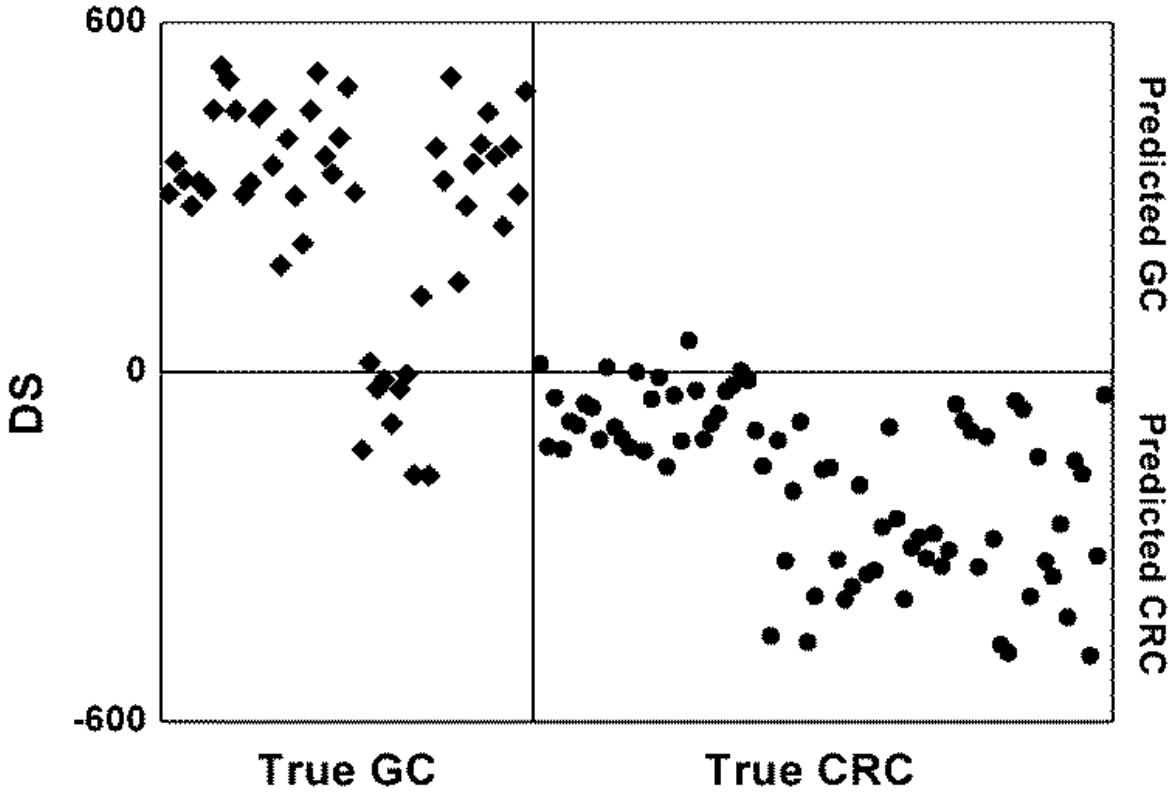

600
0
-600
DS
Predicted GC
Predicted CRC
True GC
True CRC
◆ GC / ● CRC

FIG. 48

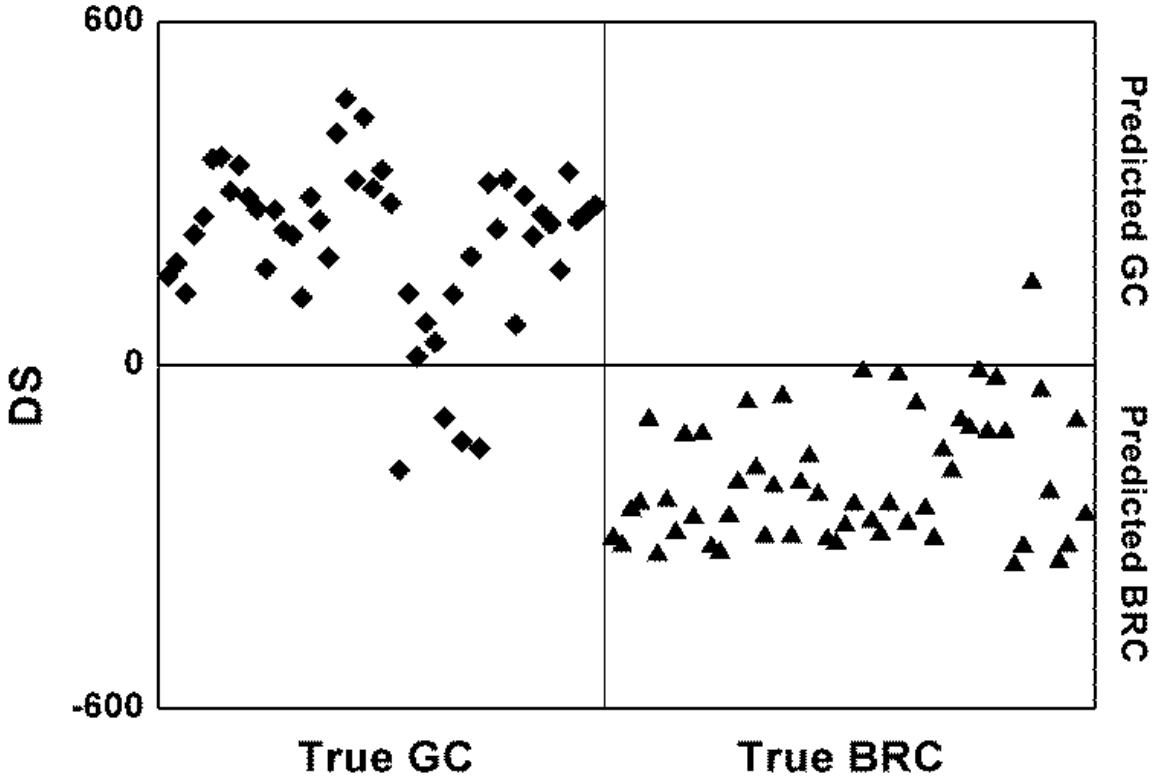
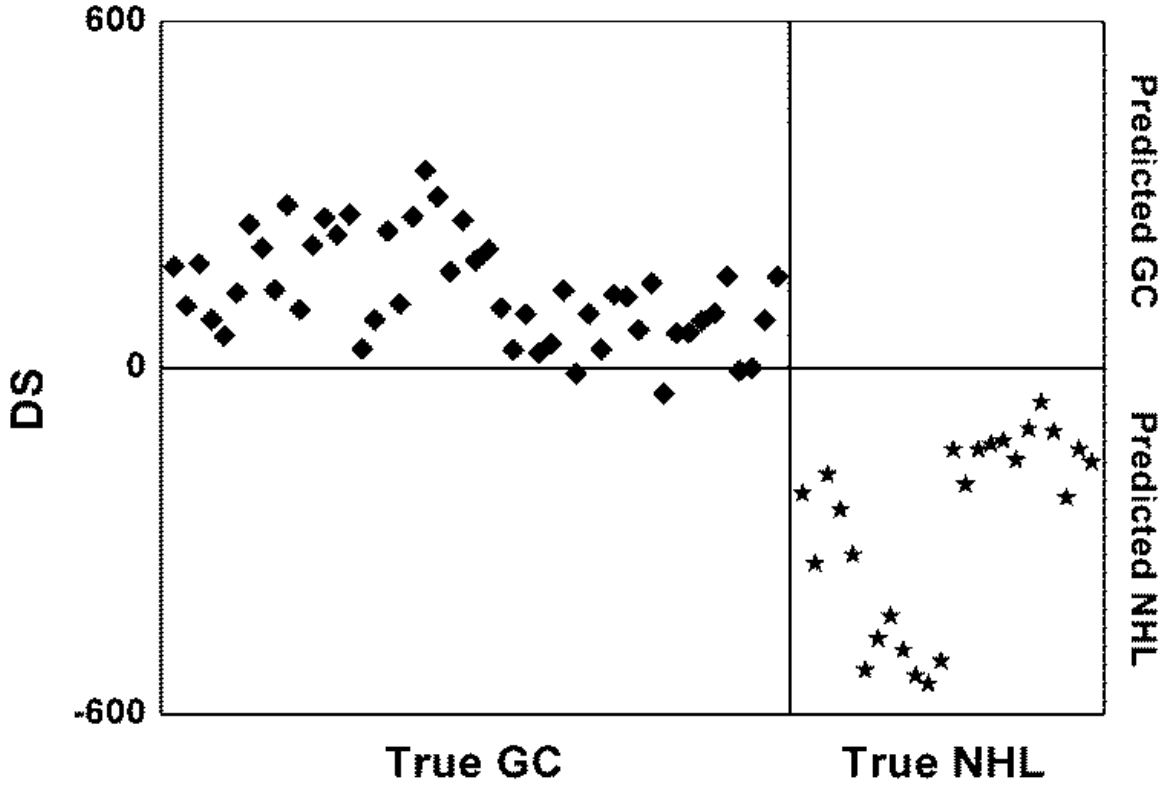

600
0
-600
DS
Predicted GC
Predicted BRC
True GC
True BRC
◆ GC / ▲ BRC

FIG. 49



◆ GC / ★ NHL

FIG. 50

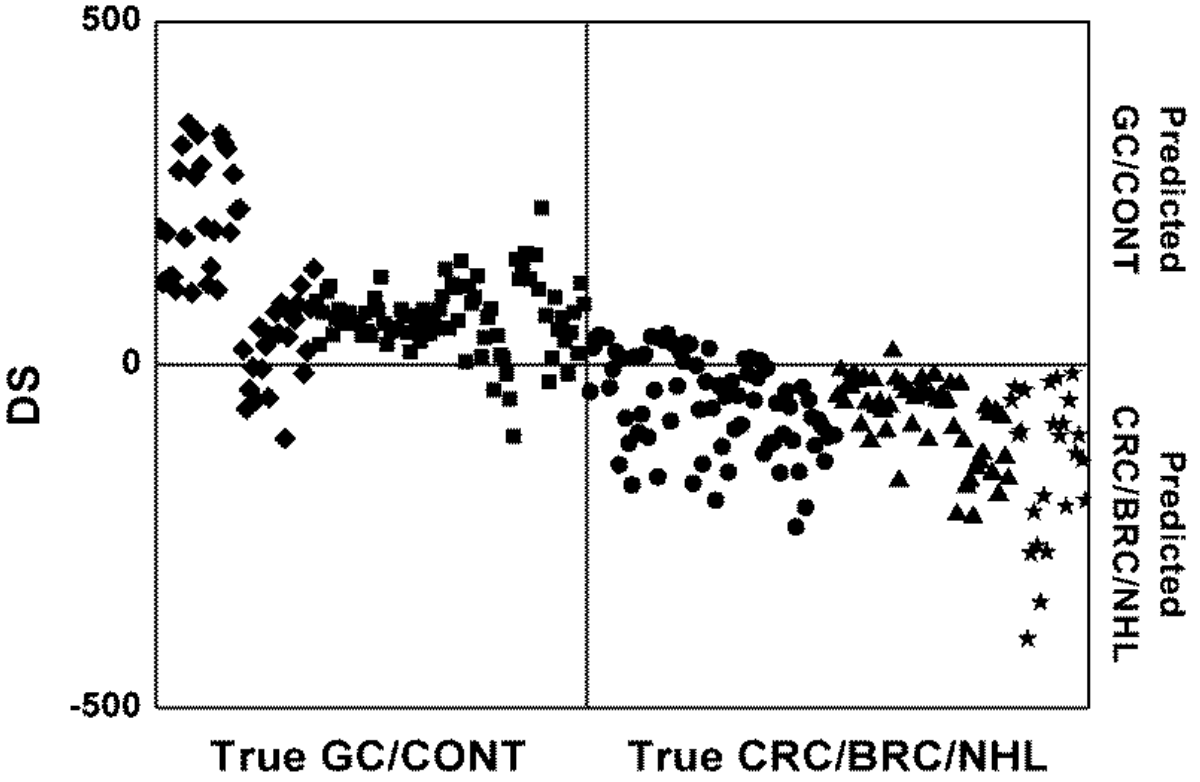

500
0
-500
DS
Predicted GC/CONT
Predicted CRC/BRC/NHL
True GC/CONT
True CRC/BRC/NHL
◆ GC / ■ CONT / ● CRC / ▲ BRC / ★ NHL

FIG. 51

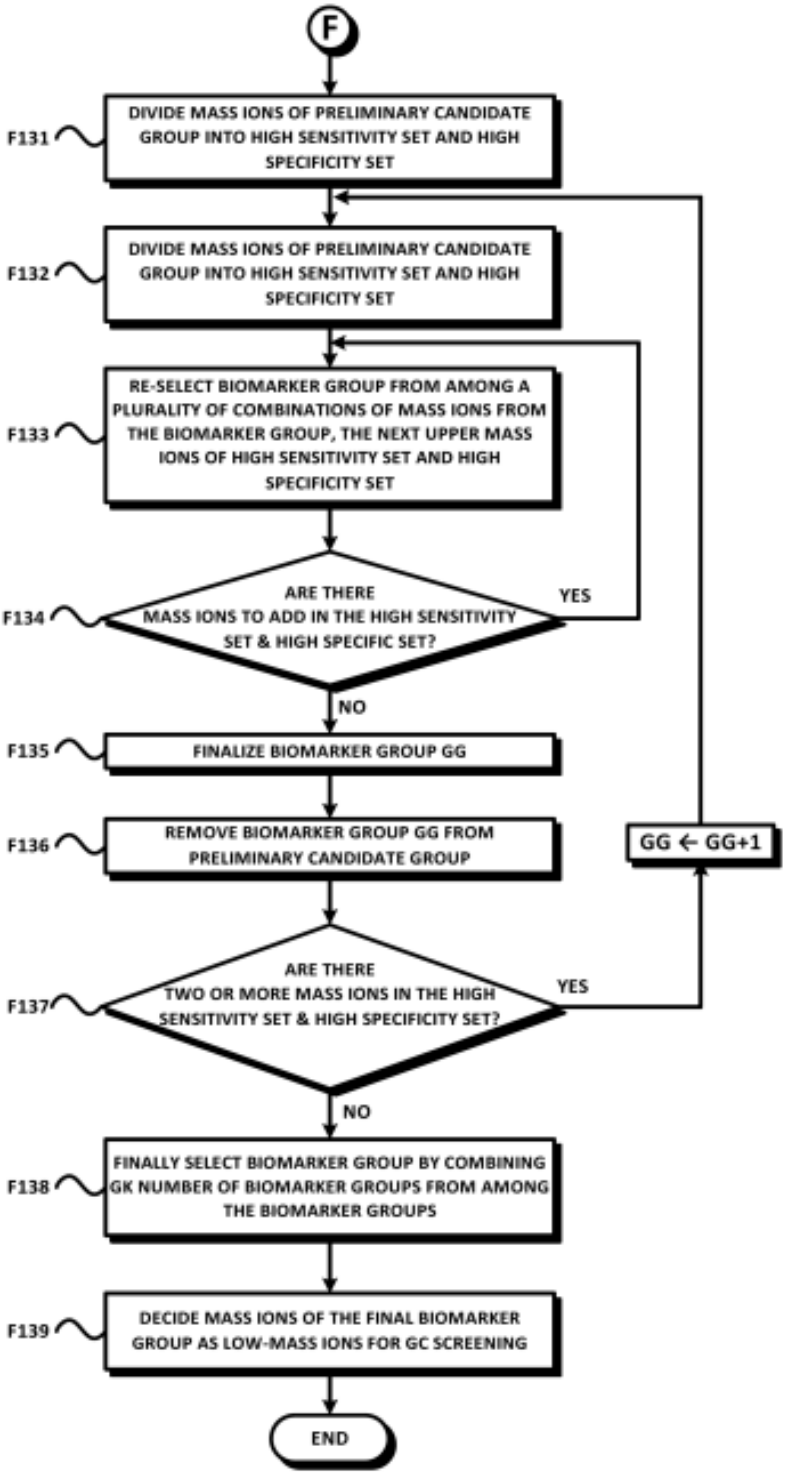

F
F131
DIVIDE MASS IONS OF PRELIMINARY CANDIDATE GROUP INTO HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
F132
DIVIDE MASS IONS OF PRELIMINARY CANDIDATE GROUP INTO HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
F133
RE-SELECT BIOMARKER GROUP FROM AMONG A PLURALITY OF COMBINATIONS OF MASS IONS FROM THE BIOMARKER GROUP, THE NEXT UPPER MASS IONS OF HIGH SENSITIVITY SET AND HIGH SPECIFICITY SET
F134
ARE THERE MASS IONS TO ADD IN THE HIGH SENSITIVITY SET & HIGH SPECIFIC SET?
YES
NO
F135
FINALIZE BIOMARKER GROUP GG
F136
REMOVE BIOMARKER GROUP GG FROM PRELIMINARY CANDIDATE GROUP
GG ← GG+1
F137
ARE THERE TWO OR MORE MASS IONS IN THE HIGH SENSITIVITY SET & HIGH SPECIFICITY SET?
YES
NO
F138
FINALLY SELECT BIOMARKER GROUP BY COMBINING GK NUMBER OF BIOMARKER GROUPS FROM AMONG THE BIOMARKER GROUPS
F139
DECIDE MASS IONS OF THE FINAL BIOMARKER GROUP AS LOW-MASS IONS FOR GC SCREENING
END

FIG. 52

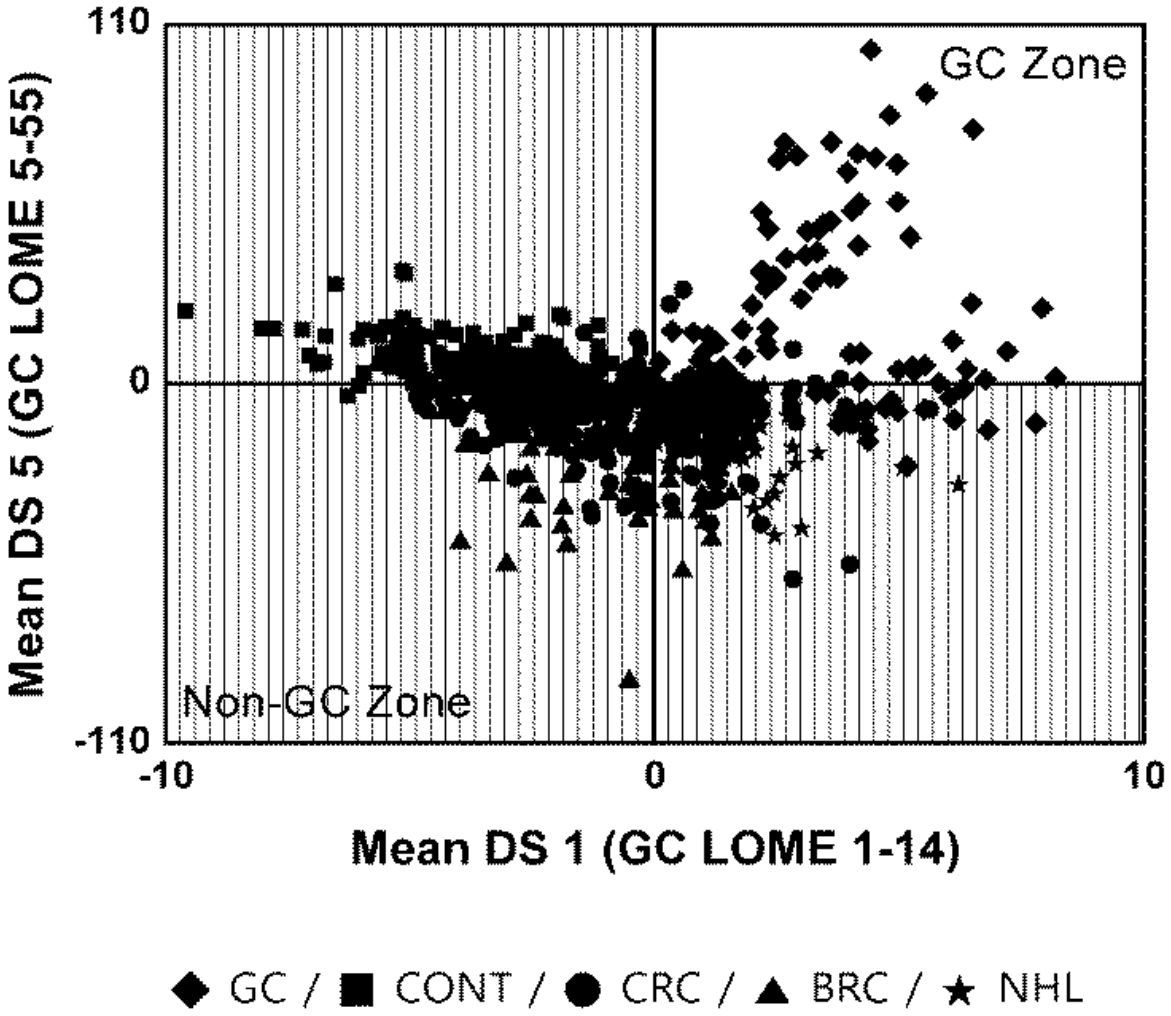

110
0
-110
-10
0
10
GC Zone
Non-GC Zone
Mean DS 5 (GC LOME 5-55)
Mean DS 1 (GC LOME 1-14)
◆ GC / ■ CONT / ● CRC / ▲ BRC / ★ NHL

FIG. 53

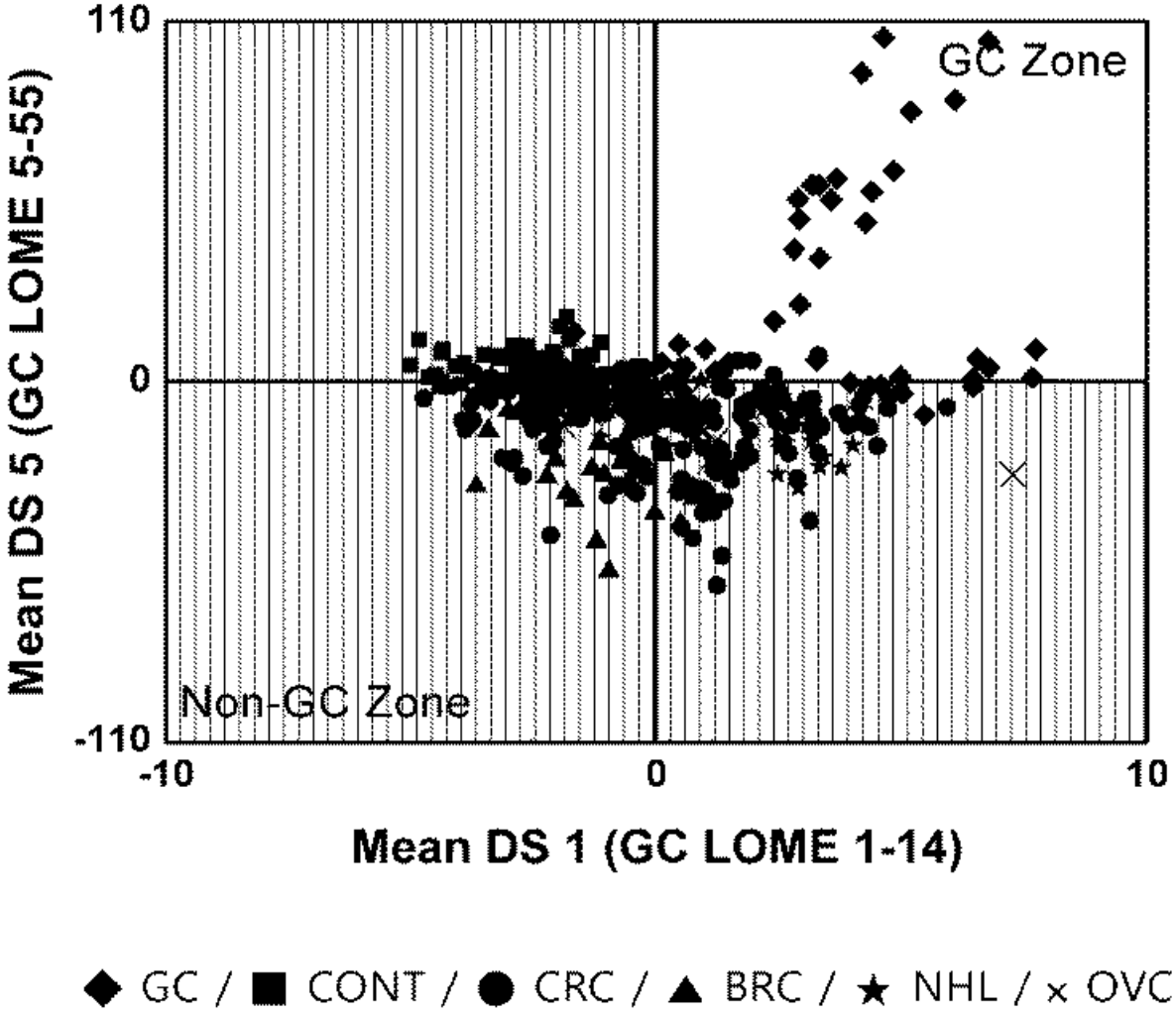

110
0
-110
-10
0
10
GC Zone
Non-GC Zone
Mean DS 5 (GC LOME 5-55)
Mean DS 1 (GC LOME 1-14)
◆ GC / ■ CONT / ● CRC / ▲ BRC / ★ NHL / x OVC

FIG. 54