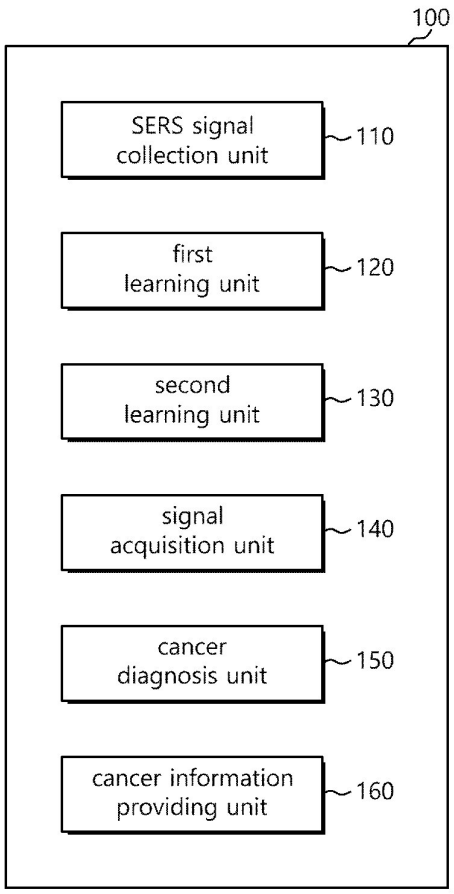
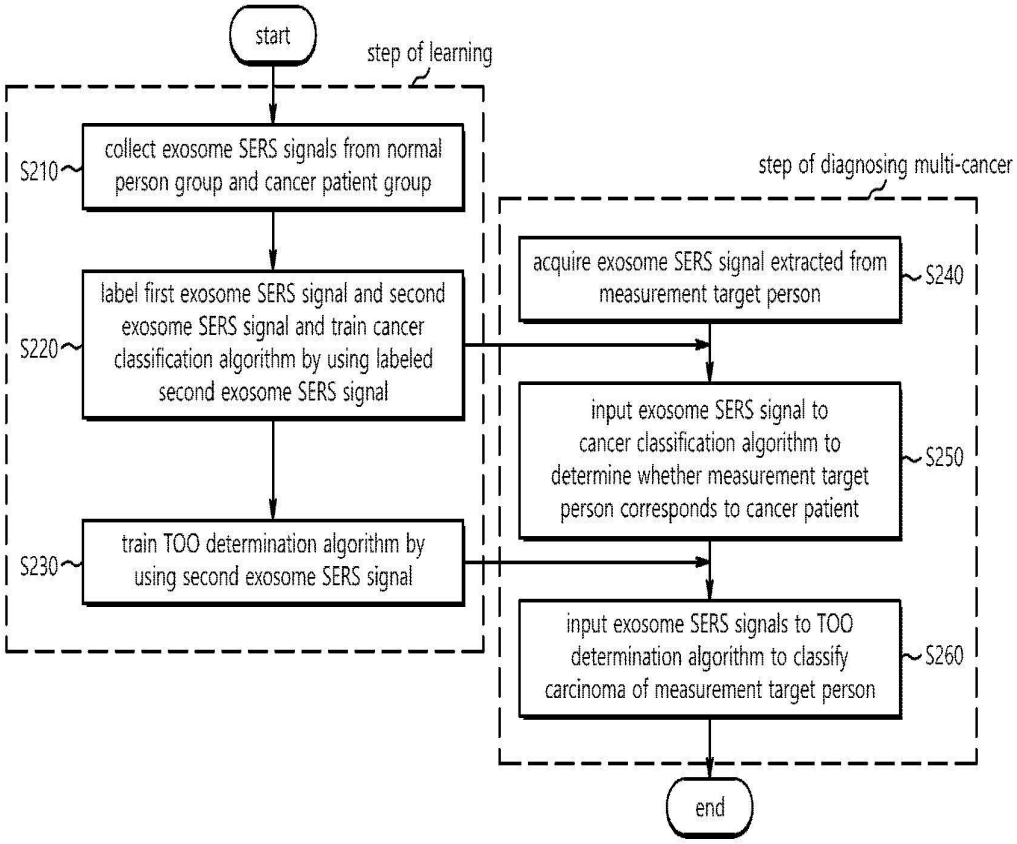
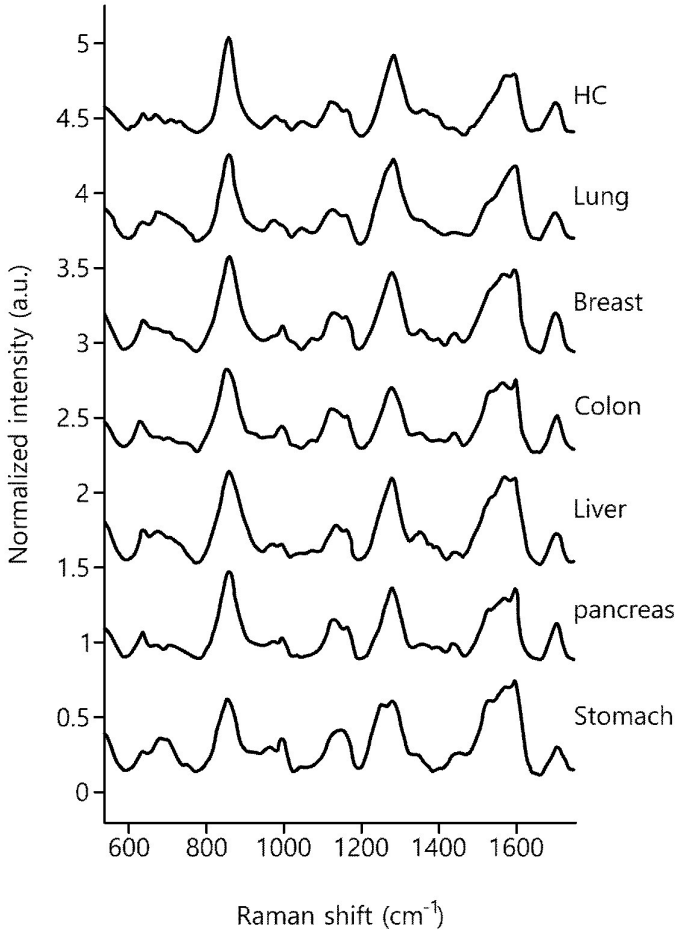
[FIG. 1]


100
SERS signal collection unit
110
first learning unit
120
second learning unit
130
signal acquisition unit
140
cancer diagnosis unit
150
cancer information providing unit
160

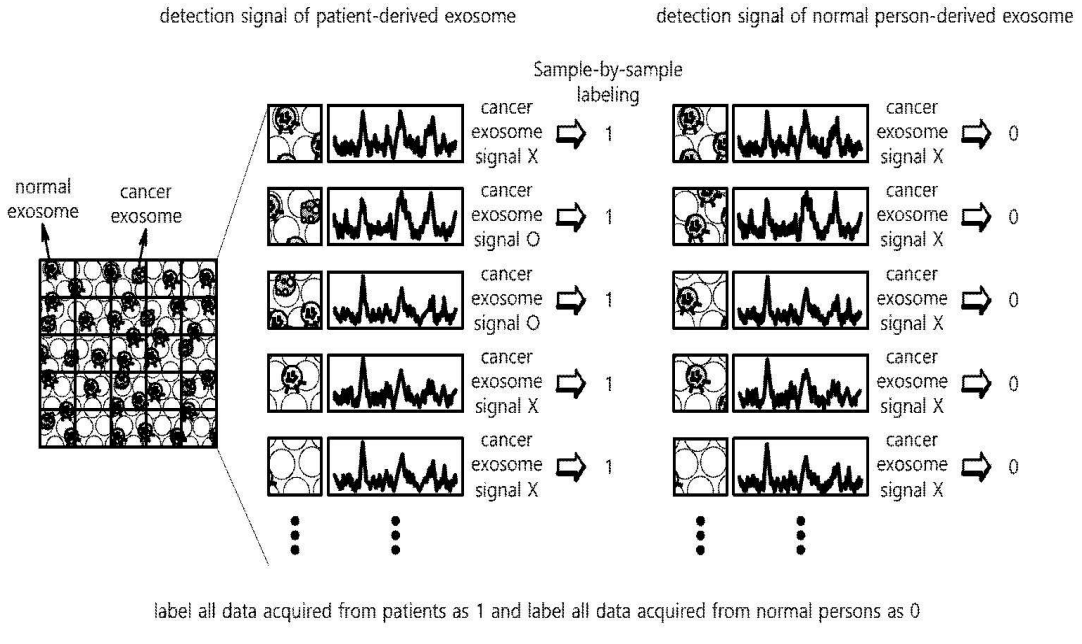
[FIG. 2]


start
step of learning
S210
collect exosome SERS signals from normal person group and cancer patient group
S220
label first exosome SERS signal and second exosome SERS signal and train cancer classification algorithm by using labeled second exosome SERS signal
S230
train TOO determination algorithm by using second exosome SERS signal
step of diagnosing multi-cancer
acquire exosome SERS signal extracted from measurement target person
S240
input exosome SERS signal to cancer classification algorithm to determine whether measurement target person corresponds to cancer patient
S250
input exosome SERS signals to TOO determination algorithm to classify carcinoma of measurement target person
S260
end

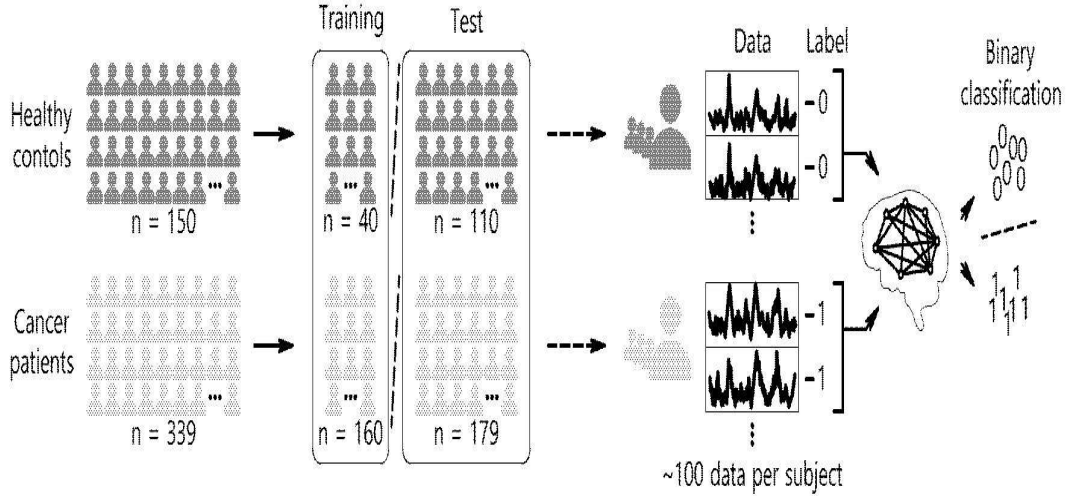
[FIG. 3]


Normalized intensity (a.u.)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
HC
Lung
Breast
Colon
Liver
pancreas
Stomach
600
800
1000
1200
1400
1600
Raman shift (cm-1)

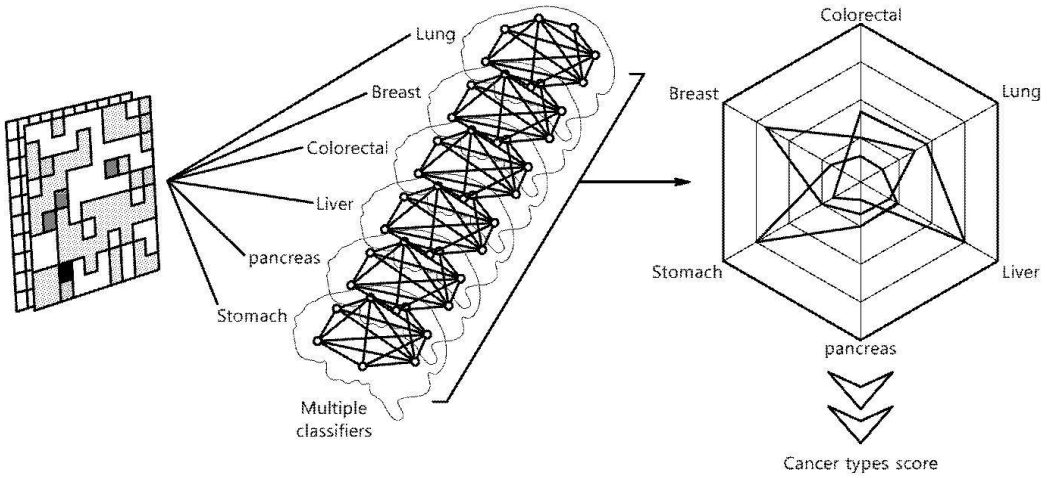
[FIG. 4]


detection signal of patient-derived exosome
detection signal of normal person-derived exosome
Sample-by-sample labeling
normal exosome
cancer exosome
cancer exosome signal X
cancer exosome signal O
1
0
label all data acquired from patients as 1 and label all data acquired from normal persons as 0

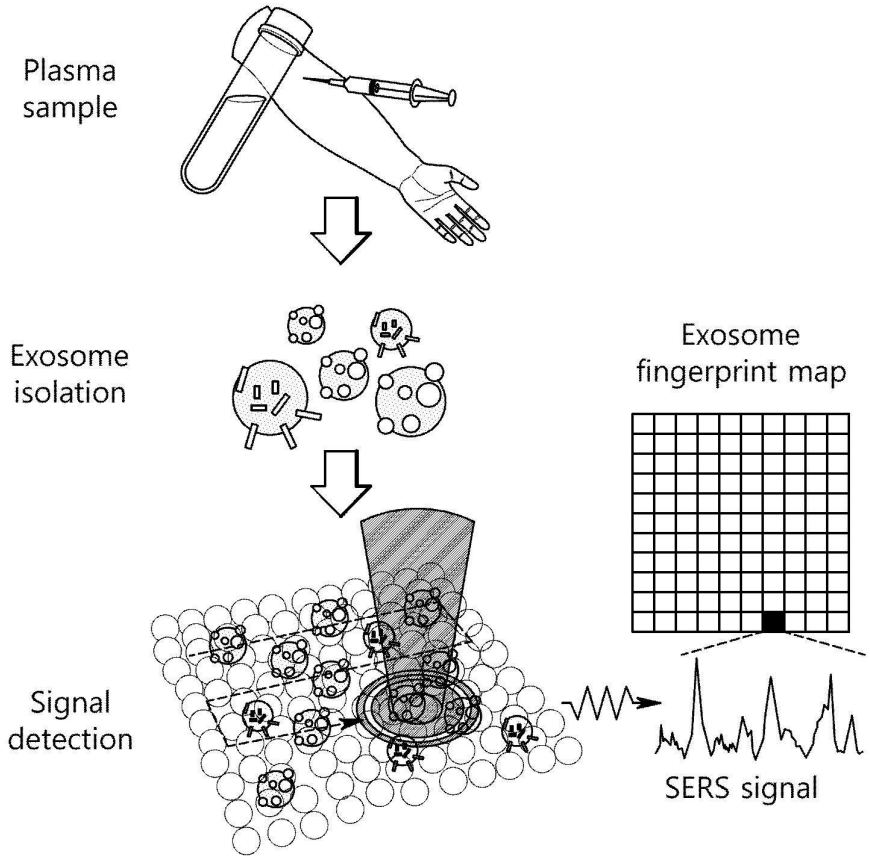
[FIG. 5]


Training
Test
Healthy contols
Cancer patients
n = 150
n = 339
n = 40
n = 160
n = 110
n = 179
Data
Label
Binary classification
-0
-1
~100 data per subject

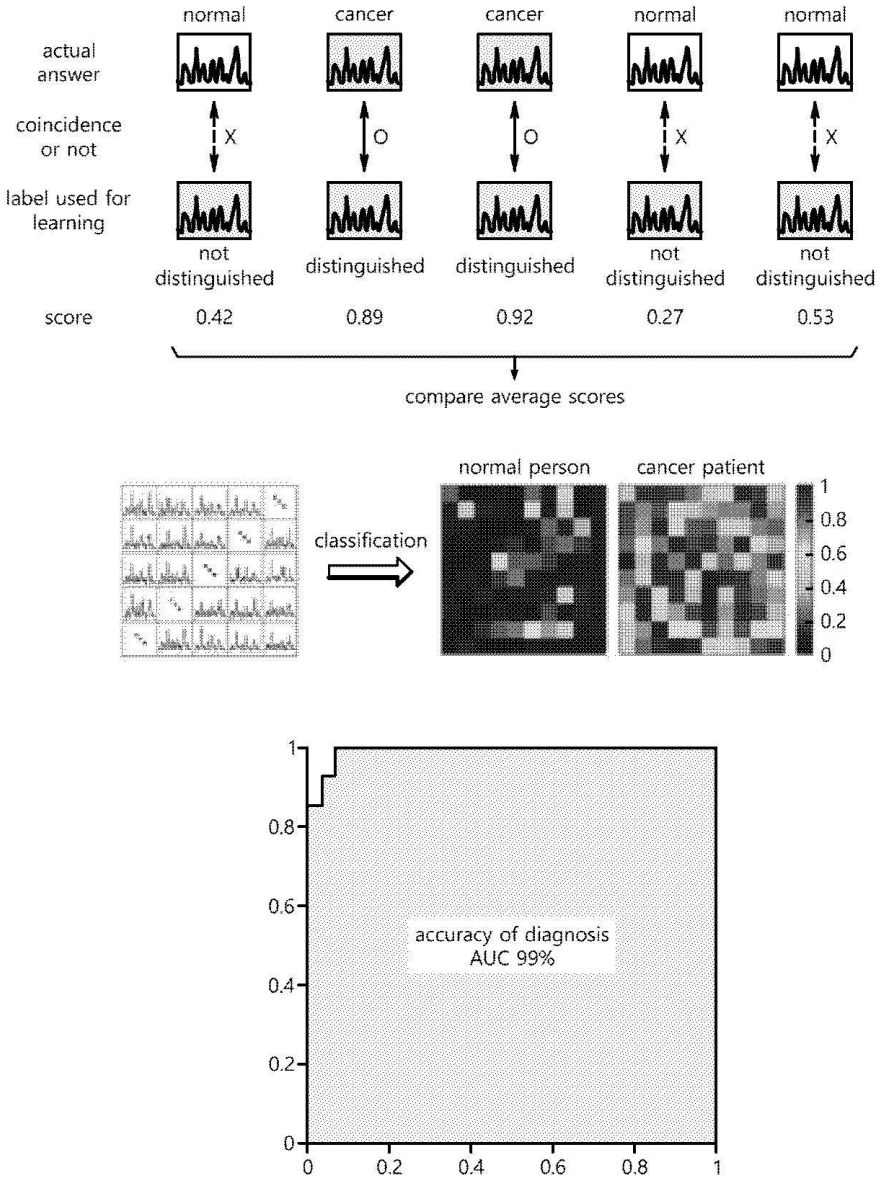
[FIG. 6]


Lung
Breast
Colorectal
Liver
pancreas
Stomach
Multiple classifiers
Colorectal
Breast
Lung
Stomach
Liver
pancreas
Cancer types score

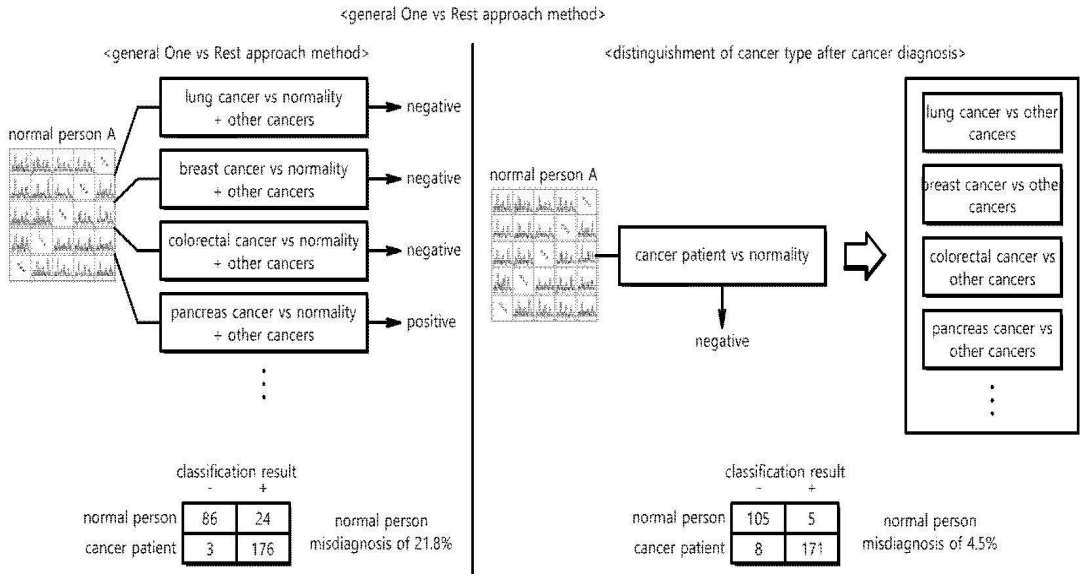
[FIG. 7]


Plasma sample
Exosome isolation
Signal detection
Exosome fingerprint map
SERS signal

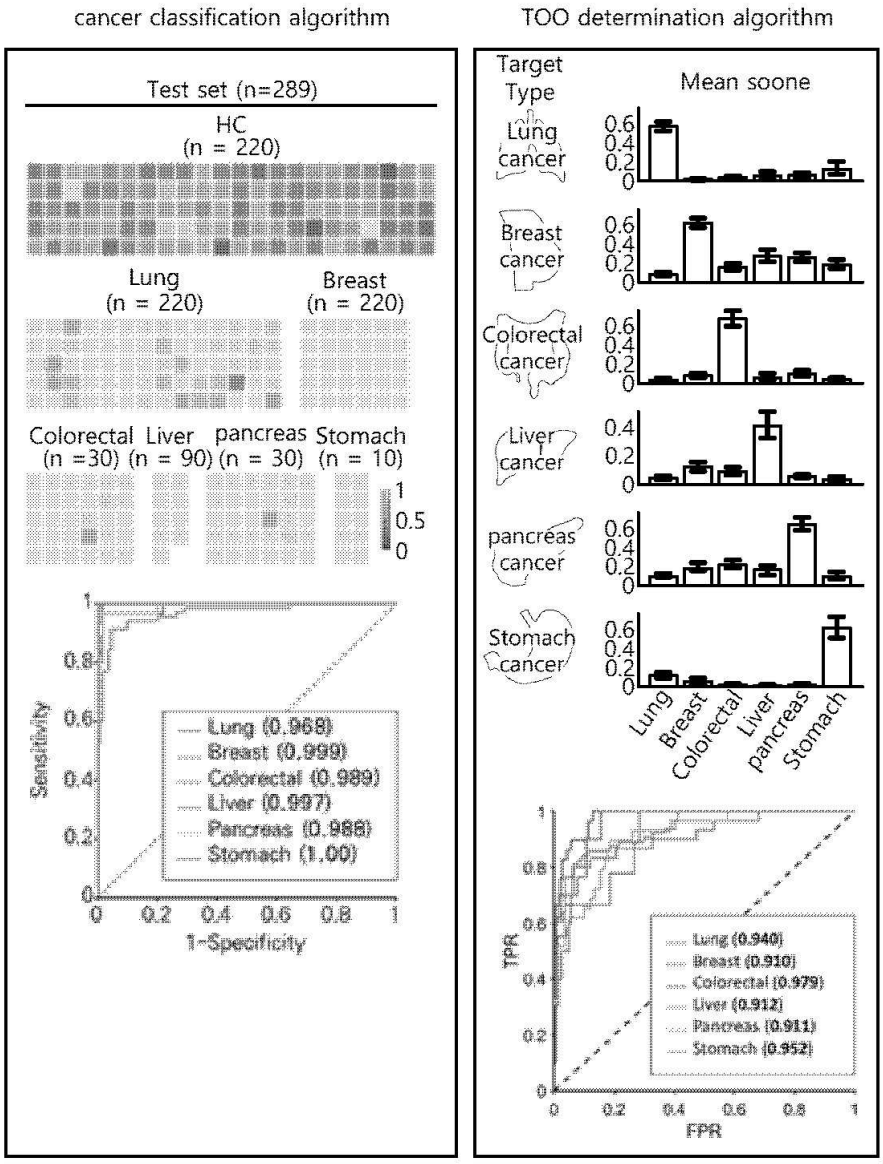
[FIG. 8]


normal
cancer
cancer
normal
normal
actual answer
coincidence or not
X
O
O
X
X
label used for learning
not distinguished
distinguished
distinguished
not distinguished
not distinguished
score
0.42
0.89
0.92
0.27
0.53
compare average scores
classification
normal person
cancer patient
1
0.8
0.6
0.4
0.2
0
accuracy of diagnosis
AUC 99%
1
0.8
0.6
0.4
0.2
0
0
0.2
0.4
0.6
0.8
1

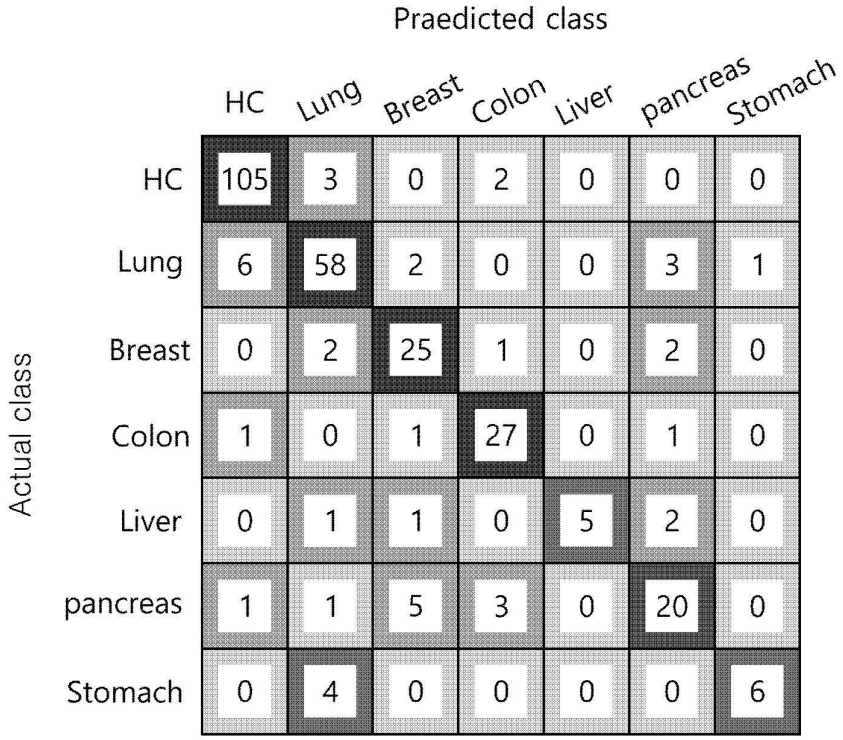
[FIG. 9]


<general One vs Rest approach method>
<general One vs Rest approach method>
normal person A
lung cancer vs normality + other cancers
negative
breast cancer vs normality + other cancers
negative
colorectal cancer vs normality + other cancers
negative
pancreas cancer vs normality + other cancers
positive
classification result
- +
normal person 86 24
cancer patient 3 176
normal person misdiagnosis of 21.8%
<distinguishment of cancer type after cancer diagnosis>
normal person A
cancer patient vs normality
negative
lung cancer vs other cancers
breast cancer vs other cancers
colorectal cancer vs other cancers
pancreas cancer vs other cancers
classification result
- +
normal person 105 5
cancer patient 8 171
normal person misdiagnosis of 4.5%

[FIG. 10]


cancer classification algorithm
TOO determination algorithm
Test set (n=289)
HC
(n = 220)
Lung
(n = 220)
Breast
(n = 220)
Colorectal
(n =30)
Liver
(n = 90)
pancreas
(n = 30)
Stomach
(n = 10)
1
0.5
0
Sensitivity
1-Specificity
Lung (0.968)
Breast (0.999)
Colorectal (0.989)
Liver (0.997)
Pancreas (0.988)
Stomach (1.00)
Target Type
Mean soone
Lung cancer
Breast cancer
Colorectal cancer
Liver cancer
pancreas cancer
Stomach cancer
Lung
Breast
Colorectal
Liver
pancreas
Stomach
TPR
FPR
Lung (0.940)
Breast (0.910)
Colorectal (0.979)
Liver (0.912)
Pancreas (0.911)
Stomach (0.952)

[FIG. 11]


Praedicted class
HC
Lung
Breast
Colon
Liver
pancreas
Stomach
Actual class
HC 105 3 0 2 0 0 0
Lung 6 58 2 0 0 3 1
Breast 0 2 25 1 0 2 0
Colon 1 0 1 27 0 1 0
Liver 0 1 1 0 5 2 0
pancreas 1 1 5 3 0 20 0
Stomach 0 4 0 0 0 0 6