Supplementary Materials

Table S1 Comparison of BBB leakage between patients with lung cancer at different stages and HCs.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | HCs(N=29) | eLCs(N=39) | aLCs(N=36) | H | P |
| CAL.L | 1.283E-03±5.090E-04 | 1.320E-03±5.120E-04 | 1.650E-03±6.100E-04 | 9.124 | 0.010 |
| SOG.L | 1.161E-03±5.640E-04 | 1.226E-03±5.320E-04 | 1.523E-03±7.360E-04 | 6.604 | 0.037 |
| SOG.R | 9.468E-04±4.010E-04 | 1.119E-03±5.140E-04 | 1.208E-03±5.030E-04 | 6.918 | 0.031 |
| MOG.R | 8.891E-04±3.660E-04 | 1.078E-03±4.020E-04 | 1.168E-03±3.520E-04 | 9.086 | 0.011 |
| IOG.L | 8.327E-04±5.410E-04 | 8.765E-04±4.410E-04 | 1.142E-03±5.790E-04 | 6.716 | 0.035 |
| IOG.R | 1.234E-03±7.140E-04 | 1.232E-03±6.680E-04 | 1.676E-03±7.340E-04 | 9.455 | 0.009 |
| TPOsup.L | 1.451E-03±4.620E-04 | 1.975E-03±7.640E-04 | 1.768E-03±8.680E-04 | 8.627 | 0.013 |
| TPOsup.R | 1.594E-03±5.030E-04 | 1.992E-03±6.550E-04 | 1.972E-03±7.210E-04 | 6.385 | 0.041 |
| TPOmid.L | 1.579E-03±7.940E-04 | 2.020E-03±7.270E-04 | 2.032E-03±1.174E-03 | 6.561 | 0.038 |
| TPOmid.R | 1.938E-03±8.610E-04 | 2.437E-03±6.600E-04 | 2.373E-03±1.014E-03 | 8.057 | 0.018 |
| Cerebelum\_Crus1\_L | 1.856E-03±6.300E-04 | 1.839E-03±6.810E-04 | 2.384E-03±9.040E-04 | 9.882 | 0.007 |
| Cerebelum\_Crus2\_L | 2.428E-03±1.211E-03 | 2.115E-03±1.046E-03 | 3.635E-03±2.650E-03 | 6.395 | 0.041 |
| Cerebelum\_6\_R | 7.005E-04±2.050E-04 | 7.119E-04±2.390E-04 | 8.212E-04±2.190E-04 | 8.193 | 0.017 |
| ktransGray | 6.601E-04±2.020E-04 | 6.875E-04±1.530E-04 | 7.788E-04±1.600E-04 | 9.610 | 0.008 |

Comparison of BBB leakage between patients with lung cancer at different stages and HCs. Data are expressed as Mean±SD. The P values are obtained by using Kruskal-Wallis Test. *CAL.L =* *Calcarine fissure and surrounding cortex，SOG.L=* *left Superior occipital gyrus; SOG.R=right Superior occipital gyrus，MOG.R=right* *Middle occipital gyrus; IOG.L=* *left Inferior occipital gyrus，IOG.R=right Inferior occipital gyrus; TPOsup.L=* *left Temporal pole: superior temporal gyrus，TPOsup.R=right Temporal pole: superior temporal gyrus，TPOmid.L=* left *Temporal pole: middle temporal gyrus，TPOmid.R=* right *Temporal pole: middle temporal gyrus，*

Table S2-15. Multiple comparisons of the group. Asymptotic significances (2-sided tests) are displayed. The significance level is 0.05.

a. Significance values have been adjusted by the Bonferroni correction for multiple tests. 1= HCs; 2= eLCs; 3= aLCs.

Table S2

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **CAL.L** | | | | | |
| Sample 1-Sample 2 | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -3.375 | 7.397 | -0.456 | 0.648 | 1.000 |
| 1-3 | -20.501 | 7.527 | -2.724 | 0.006 | 0.019 |
| 2-3 | -17.126 | 6.972 | -2.456 | 0.014 | 0.042 |

Table S3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SOG.L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -3.676 | 7.397 | -0.497 | 0.619 | 1.000 |
| 1-3 | -17.784 | 7.527 | -2.363 | 0.018 | 0.054 |
| 2-3 | -14.109 | 6.972 | -2.024 | 0.043 | 0.129 |

Table S4

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SOG.R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -11.870 | 7.397 | -1.605 | 0.109 | 0.326 |
| 1-3 | -19.765 | 7.527 | -2.626 | 0.009 | 0.026 |
| 2-3 | -7.895 | 6.972 | -1.132 | 0.257 | 0.772 |

Table S5

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **MOG.R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -14.022 | 7.397 | -1.896 | 0.058 | 0.174 |
| 1-3 | -22.614 | 7.527 | -3.004 | 0.003 | 0.008 |
| 2-3 | -8.592 | 6.972 | -1.232 | 0.218 | 0.653 |

Table S6

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **IOG.L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -3.985 | 7.397 | -.539 | 0.590 | 1.000 |
| 1-3 | -18.047 | 7.527 | -2.398 | 0.017 | 0.050 |
| 2-3 | -14.062 | 6.972 | -2.017 | 0.044 | 0.131 |

Table S7

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **IOG.R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | .205 | 7.397 | .028 | 0.978 | 1.000 |
| 1-3 | -19.000 | 7.527 | -2.524 | 0.012 | 0.035 |
| 2-3 | -19.205 | 6.972 | -2.755 | 0.006 | 0.018 |

Table S8

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **TPOsup.L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -21.637 | 7.397 | -2.925 | 0.003 | 0.010 |
| 1-3 | -14.066 | 7.527 | -1.869 | 0.062 | 0.185 |
| 2-3 | 7.571 | 6.972 | 1.086 | 0.278 | 0.833 |

Table S9

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **TPOsup.R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -16.462 | 7.527 | -2.187 | 0.029 | 0.086 |
| 1-3 | -16.851 | 7.397 | -2.278 | 0.023 | 0.068 |
| 2-3 | .389 | 6.972 | 0.056 | 0.956 | 1.000 |

Table S10

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **TPOmid.L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -18.379 | 7.397 | -2.485 | 0.013 | 0.039 |
| 1-3 | -14.407 | 7.527 | -1.914 | 0.056 | 0.167 |
| 2-3 | 3.972 | 6.972 | 0.570 | 0.569 | 1.000 |

Table S11

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **TPOmid.R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -20.713 | 7.397 | -2.800 | 0.005 | 0.015 |
| 1-3 | -14.768 | 7.527 | -1.962 | 0.050 | 0.149 |
| 2-3 | 5.944 | 6.972 | 0.853 | 0.394 | 1.000 |

Table S12

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cerebelum\_Crus1\_L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | 2.214 | 7.397 | 0.299 | 0.765 | 1.000 |
| 1-3 | -20.402 | 6.972 | -2.926 | 0.003 | 0.010 |
| 2-3 | -18.188 | 7.527 | -2.416 | 0.016 | 0.047 |

Table S13

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cerebelum\_Crus2\_L** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 2-1 | 6.368 | 7.397 | 0.861 | 0.389 | 1.000 |
| 2-3 | -17.500 | 6.972 | -2.510 | 0.012 | 0.036 |
| 1-3 | -11.132 | 7.527 | -1.479 | 0.139 | 0.417 |

Table S14

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cerebelum\_6\_R** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -1.397 | 7.397 | -0.189 | .850 | 1.000 |
| 1-3 | -18.559 | 7.527 | -2.466 | .014 | 0.041 |
| 2-3 | -17.162 | 6.972 | -2.462 | .014 | .042 |

Table S15

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ktransGray** | | | | | |
|  | Test Statistic | Std. Error | Std. Test Statistic | Sig. | Adj. Sig.a |
| 1-2 | -5.789 | 7.397 | -.783 | .434 | 1.000 |
| 1-3 | -21.970 | 7.527 | -2.919 | .004 | .011 |
| 2-3 | -16.182 | 6.972 | -2.321 | .020 | .061 |

Table S17.Correlation between tumor markers, diameter, and BBB leakage in patients with LC

|  |  |  |  |
| --- | --- | --- | --- |
| BBB | tumor markers and diameter | R | P |
| Calcarine\_L | CYFRA21-1 | 0.266 | 0.021 |
| Temporal\_Pole\_Mid\_L |  | 0.449 | 0.000 |
| Temporal\_Pole\_Mid\_R |  | 0.508 | 0.000 |
| Cerebelum\_Crus1\_L |  | 0.303 | 0.008 |
| Cerebelum\_6\_R |  | 0.342 | 0.003 |
| ktransGray |  | 0.305 | 0.008 |
| ktransGray | CEA | 0.228 | 0.049 |
| Calcarine\_L | Tumor diameter | 0.257 | 0.026 |
| Occipital\_Inf\_L |  | 0.239 | 0.039 |
| Occipital\_Inf\_R |  | 0.298 | 0.009 |
| Temporal\_Pole\_Mid\_L |  | 0.599 | 0.000 |
| Temporal\_Pole\_Mid\_R |  | 0.659 | 0.000 |
| Cerebelum\_Crus1\_L |  | 0.329 | 0.004 |
| Cerebelum\_Crus2\_L |  | 0.299 | 0.009 |

The P values are obtained by using spearman correlation analysis, The correlation is significant at the 0.05 level.

Table S18.Correlation between tumor markers, diameter, and cognitive function in patients with LC

|  |  |  |  |
| --- | --- | --- | --- |
| tumor markers, diameter | cognitive function | R | P |
| Tumor diameter | visuospatial/executive | -0.23 | 0.050 |
|  | delayed recall | -0.33 | 0.004 |
|  | total score | -0.36 | 0.002 |
| CYFRA21-1 | visuospatial/executive | -0.28 | 0.016 |
|  | total score | -0.33 | 0.004 |

The P values are obtained by using spearman correlation analysis, The correlation is significant at the 0.05 level.

Table S19.Correlation between cognitive function and BBB leakage in patients with LC

|  |  |  |  |
| --- | --- | --- | --- |
| BBB | cognitive function | R | P |
| Temporal\_Pole\_Mid\_L | visuospatial/executive | -0.259 | 0.025 |
| Temporal\_Pole\_Mid\_R |  | -0.263 | 0.022 |
| Cerebelum\_6\_R |  | -0.325 | 0.004 |
| Temporal\_Pole\_Mid\_R | delayed recall | -0.256 | 0.027 |
| Cerebelum\_6\_R |  | -0.307 | 0.007 |
| Temporal\_Pole\_Mid\_L | total score | -0.269 | 0.020 |
| Temporal\_Pole\_Mid\_R |  | -0.274 | 0.017 |
| Cerebelum\_6\_R |  | -0.394 | 0.000 |
| ktransGray |  | -0.252 | 0.029 |

The P values are obtained by using spearman correlation analysis, The correlation is significant at the 0.05 level.

*Calcarine\_L, calcarine fissure and surrounding cortex, CAL.L; Temporal\_Pole\_Mid\_L, left temporal pole: middle temporal gyrus, TPOmid.L; Temporal\_Pole\_Mid\_R, right temporal pole: middle temporal gyrus, TPOmid.R; KtransGray, the Ktrans for the whole brain gray; Occipital\_Inf\_L,* *left inferior occipital gyrus, IOG.L; Occipital\_Inf\_R, right inferior occipital gyrus, IOG.R; Cerebelum\_Crus1\_L, left cerebellum superior 1; Cerebelum\_Crus2\_L, left cerebellum inferior 2; Cerebelum\_6\_R, right cerebellum superior 6*