

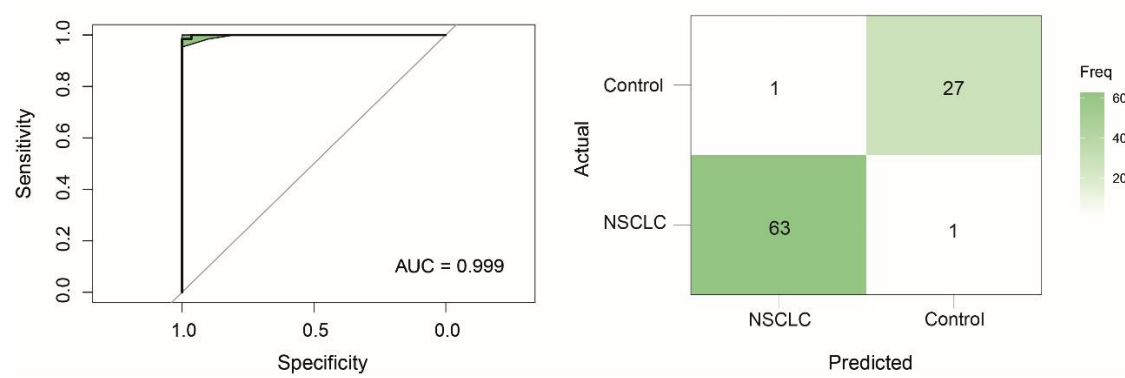
**Table S1.** Plasma metabolite profiles of the control group and non-small cell lung cancer (NSCLC) patients pre-radiation therapy.

|                                                | Control group       | All NSCLC patients  | p-value |
|------------------------------------------------|---------------------|---------------------|---------|
| Plasma metabolites                             | <i>n</i> = 40       | <i>n</i> = 91       |         |
| Pyruvic acid                                   | 6.11 [5.06-7.46]    | 6.40 [4.72-8.46]    | 0.725   |
| Lactic acid                                    | 15.93 [13.27-17.39] | 14.28 [12.56-16.91] | 0.202   |
| 2-Hydroxyisobutyric acid                       | 0.33 [0.27-0.42]    | 0.44 [0.35-0.65]    | <0.001  |
| Glycolic acid                                  | 0.26 [0.23-0.28]    | 0.19 [0.16-0.23]    | <0.001  |
| Alanine                                        | 2.80 [2.34-3.49]    | 2.91 [2.53-3.49]    | 0.357   |
| 2-Hydroxybutyric acid                          | 4.38 [3.60-5.76]    | 4.02 [2.86-5.58]    | 0.205   |
| 3-methyl-2-oxobutyric acid                     | 0.17 [0.13-0.20]    | 0.11 [0.09-0.15]    | <0.001  |
| 3-hydroxybutyric acid/3-hydroxyisobutyric acid | 1.88 [1.35-2.67]    | 1.59 [0.89-4.44]    | 0.518   |
| 2-Hydroxyisovaleric acid                       | 1.29 [1.03-1.64]    | 1.50 [1.08-2.74]    | 0.093   |
| 2-keto-3-methylvaleric acid                    | 0.30 [0.23-0.34]    | 0.22 [0.17-0.28]    | <0.001  |
| 3-Hydroxyisovaleric acid                       | 0.25 [0.21-0.30]    | 0.30 [0.21-0.36]    | 0.043   |
| Valine                                         | 18.91 [17.34-20.69] | 17.29 [14.90-20.19] | 0.006   |
| Benzoic acid                                   | 0.26 [0.18-0.35]    | 0.25 [0.20-0.34]    | 0.974   |
| Ethanolamine                                   | 0.33 [0.28-0.38]    | 0.29 [0.25-0.36]    | 0.136   |
| Leucine                                        | 10.00 [9.32-11.28]  | 8.99 [7.23-10.85]   | 0.001   |
| Phosphoric acid                                | 3.83 [2.99-4.83]    | 3.73 [2.88-4.39]    | 0.449   |
| Glycerol                                       | 2.44 [1.72-3.16]    | 0.80 [0.51-1.25]    | <0.001  |
| Ethylmalonic acid                              | 3.74 [2.79-4.33]    | 1.02 [0.75-1.44]    | <0.001  |
| Isoleucine                                     | 5.40 [4.79-6.01]    | 4.70 [3.95-5.85]    | 0.027   |
| Proline                                        | 20.83 [17.32-28.22] | 22.19 [14.21-30.23] | 0.863   |
| Glycine                                        | 1.26 [1.20-1.36]    | 1.26 [1.15-1.36]    | 0.405   |
| Succinic acid                                  | 0.08 [0.07-0.09]    | 0.10 [0.09-0.13]    | <0.001  |
| Glyceric acid                                  | 0.58 [0.52-0.74]    | 0.70 [0.56-0.93]    | 0.022   |
| Fumaric acid                                   | 0.52 [0.38-0.74]    | 0.42 [0.25-0.61]    | 0.049   |
| Serine                                         | 7.30 [5.90-7.96]    | 5.87 [4.89-7.20]    | 0.004   |
| Threonine                                      | 7.68 [6.56-8.83]    | 6.71 [5.71-8.01]    | 0.014   |
| Hydrocinnamic acid                             | 0.15 [0.08-0.23]    | 0.11 [0.07-0.18]    | 0.196   |
| Malic acid                                     | 0.09 [0.08-0.12]    | 0.14 [0.10-0.19]    | <0.001  |
| d-Threitol                                     | 0.02 [0.02-0.03]    | 0.03 [0.03-0.04]    | <0.001  |
| Methionine                                     | 1.91 [1.77-2.09]    | 1.61 [1.29-1.98]    | <0.001  |
| Oxoproline                                     | 50.23 [42.98-56.01] | 61.32 [49.51-69.37] | <0.001  |
| 4-Hydroxyproline                               | 1.75 [1.26-2.67]    | 1.71 [1.27-2.33]    | 0.836   |
| Threonic acid                                  | 1.66 [1.51-1.94]    | 2.40 [1.79-3.55]    | <0.001  |
| Erythronic acid                                | 0.06 [0.05-0.09]    | 0.11 [0.08-0.22]    | <0.001  |
| DL-2-Hydroxyglutaric acid                      | 0.05 [0.04-0.05]    | 0.06 [0.05-0.08]    | <0.001  |
| α-ketoglutaric acid                            | 0.80 [0.69-0.93]    | 0.73 [0.59-0.87]    | 0.026   |
| Glutamic acid                                  | 3.59 [2.73-4.86]    | 8.07 [5.55-10.34]   | <0.001  |
| 4-Hydroxybenzoic acid                          | 0.02 [0.02-0.03]    | 0.03 [0.03-0.05]    | <0.001  |
| Phenylalanine                                  | 6.81 [6.43-7.27]    | 6.60 [5.56-7.72]    | 0.285   |
| Dodecanoic acid                                | 0.22 [0.16-0.29]    | 0.23 [0.17-0.33]    | 0.284   |
| d-Xylose                                       | 0.03 [0.03-0.06]    | 0.05 [0.04-0.08]    | <0.001  |
| Taurine                                        | 0.62 [0.45-0.82]    | 1.33 [0.91-1.73]    | <0.001  |
| d-Arabinose                                    | 0.08 [0.06-0.09]    | 0.14 [0.11-0.23]    | <0.001  |
| d-Xylitol                                      | 0.00 [0.00-0.00]    | 0.00 [0.00-0.00]    | <0.001  |
| d-Arabitol                                     | 0.02 [0.01-0.02]    | 0.02 [0.02-0.03]    | <0.001  |
| Glycerol-1-phosphate                           | 0.06 [0.06-0.08]    | 0.07 [0.05-0.09]    | 0.380   |
| Glutamine                                      | 41.02 [35.52-50.56] | 27.16 [14.54-38.64] | <0.001  |
| Xylonic acid                                   | 0.14 [0.10-0.18]    | 0.05 [0.04-0.11]    | <0.001  |

|                            |                      |                      |                  |
|----------------------------|----------------------|----------------------|------------------|
| Ribonic acid               | 0.01 [0.01-0.01]     | 0.02 [0.01-0.04]     | <b>&lt;0.001</b> |
| 3-Phosphoglyceric acid     | 0.01 [0.01-0.01]     | 0.03 [0.02-0.05]     | <b>&lt;0.001</b> |
| Ornithine                  | 21.03 [16.59-24.92]  | 16.81 [13.13-23.86]  | <b>0.009</b>     |
| Citric acid                | 87.69 [68.20-110.80] | 86.26 [58.21-125.49] | 0.867            |
| Tetradecanoic acid         | 1.03 [0.81-1.34]     | 1.03 [0.72-1.37]     | 0.537            |
| Hippuric acid              | 1.01 [0.71-2.20]     | 0.91 [0.30-1.89]     | 0.275            |
| Vanillylmandelic acid      | 0.02 [0.01-0.02]     | 0.03 [0.02-0.04]     | <b>&lt;0.001</b> |
| 4-hydroxyPhenyllactic acid | 2.16 [1.67-2.56]     | 2.36 [1.86-3.23]     | 0.229            |
| d-Fructose                 | 0.03 [0.03-0.04]     | 0.05 [0.03-0.14]     | <b>&lt;0.001</b> |
| d-Mannitol                 | 0.03 [0.02-0.06]     | 0.14 [0.07-0.51]     | <b>&lt;0.001</b> |
| d-Mannonic acid            | 0.07 [0.05-0.10]     | 0.16 [0.11-0.30]     | <b>&lt;0.001</b> |
| d-Galactitol               | 0.02 [0.02-0.03]     | 0.02 [0.02-0.03]     | 0.519            |
| Galacturonic acid          | 0.05 [0.04-0.06]     | 0.07 [0.05-0.12]     | <b>&lt;0.001</b> |
| Galactonic acid            | 0.00 [0.00-0.01]     | 0.01 [0.00-0.02]     | <b>&lt;0.001</b> |
| Saccharic acid             | 0.04 [0.03-0.07]     | 0.08 [0.05-0.13]     | <b>&lt;0.001</b> |
| Indole-3-propanoic acid    | 0.09 [0.05-0.17]     | 0.06 [0.03-0.09]     | <b>0.001</b>     |
| Myo-Inositol               | 0.64 [0.55-0.70]     | 0.89 [0.71-1.08]     | <b>&lt;0.001</b> |
| Uric acid                  | 12.86 [7.95-16.96]   | 12.55 [7.92-16.87]   | 0.974            |
| Sedoheptulose              | 0.05 [0.04-0.06]     | 0.07 [0.05-0.09]     | <b>&lt;0.001</b> |
| Indolelactic acid          | 0.32 [0.28-0.47]     | 0.50 [0.39-0.61]     | <b>&lt;0.001</b> |
| Linoleic acid              | 1.83 [1.39-3.40]     | 1.39 [0.86-2.59]     | <b>0.008</b>     |
| Oleic acid                 | 11.46 [8.53-16.61]   | 9.83 [5.38-17.30]    | 0.096            |
| Glucose 6-phosphate        | 0.00 [0.00-0.00]     | 0.01 [0.01-0.01]     | <b>&lt;0.001</b> |
| d-Sucrose                  | 0.02 [0.01-0.03]     | 0.07 [0.04-0.15]     | <b>&lt;0.001</b> |
| Maltose                    | 0.01 [0.01-0.01]     | 0.12 [0.05-0.22]     | <b>&lt;0.001</b> |
| $\alpha$ -Tocopherol       | 0.44 [0.31-0.56]     | 0.42 [0.27-0.60]     | 0.574            |

Results are presented in Relative Units (RU) and displayed as medians [interquartile ranges]. Statistical differences were assessed using the Mann-Whitney U test on the  $\log_{10}$  RU.

**Figure S1.** Receiver Operating Characteristic (ROC) curve and confusion matrix generated using the training set of the data and a 5-fold cross validated Support Vector Machine model based on the 8 selected metabolites. The model distinguishes between non-small cell lung cancer patients (NSCLC) and the control group. AUC: Area under the curve



**Table S2.** Plasma metabolite profiles of non-small cell lung cancer (NSCLC) patients pre- and post- SBRT.

|                                                | Pre - SBRT           | Post - SBRT          | p-value      |
|------------------------------------------------|----------------------|----------------------|--------------|
| Plasma metabolites                             | <i>n</i> = 45        | <i>n</i> = 45        |              |
| Pyruvic acid                                   | 6.18 [4.91, 7.79]    | 4.83 [3.56, 7.19]    | 0.052        |
| Lactic acid                                    | 14.61 [12.94, 17.27] | 13.68 [11.86, 15.70] | <b>0.028</b> |
| 2-Hydroxyisobutyric acid                       | 0.45 [0.37, 0.64]    | 0.52 [0.37, 0.71]    | 0.495        |
| Glycolic acid                                  | 0.20 [0.17, 0.22]    | 0.18 [0.16, 0.22]    | 0.297        |
| Alanine                                        | 2.94 [2.62, 3.56]    | 2.87 [2.56, 3.53]    | 0.346        |
| 2-Hydroxybutyric acid                          | 3.98 [2.88, 5.72]    | 3.75 [2.36, 4.89]    | 0.105        |
| 3-methyl-2-oxobutyric acid                     | 0.11 [0.09, 0.14]    | 0.11 [0.09, 0.15]    | 0.947        |
| 3-hydroxybutyric acid/3-hydroxyisobutyric acid | 2.07 [0.99, 6.44]    | 2.11 [1.26, 3.99]    | 0.687        |
| 2-Hydroxyisovaleric acid                       | 1.57 [1.13, 2.58]    | 1.62 [1.06, 2.17]    | 0.200        |
| 2-keto-3-methylvaleric acid                    | 0.21 [0.17, 0.27]    | 0.20 [0.16, 0.26]    | 0.395        |
| 3-Hydroxyisovaleric acid                       | 0.30 [0.24, 0.34]    | 0.29 [0.22, 0.33]    | 0.313        |
| Valine                                         | 17.68 [15.62, 20.25] | 18.20 [15.55, 20.60] | 1.000        |
| Benzoic acid                                   | 0.30 [0.22, 0.38]    | 0.26 [0.20, 0.37]    | 0.341        |
| Ethanolamine                                   | 0.30 [0.25, 0.35]    | 0.29 [0.27, 0.35]    | 0.576        |
| Leucine                                        | 9.39 [7.90, 11.13]   | 9.13 [8.13, 10.79]   | 0.553        |
| Phosphoric acid                                | 3.62 [2.78, 4.12]    | 3.88 [3.04, 4.32]    | 0.440        |
| Glycerol                                       | 0.94 [0.68, 1.31]    | 0.85 [0.70, 1.24]    | 0.754        |
| Ethylmalonic acid                              | 1.16 [0.79, 1.42]    | 1.01 [0.84, 1.20]    | 0.297        |
| Isoleucine                                     | 5.16 [3.95, 6.09]    | 4.95 [4.18, 6.21]    | 0.938        |
| Proline                                        | 23.07 [13.62, 28.29] | 19.91 [12.78, 29.03] | 0.788        |
| Glycine                                        | 1.31 [1.17, 1.40]    | 1.29 [1.24, 1.37]    | 0.257        |
| Succinic acid                                  | 0.10 [0.09, 0.14]    | 0.10 [0.08, 0.13]    | 0.061        |
| Glyceric acid                                  | 0.66 [0.55, 0.89]    | 0.65 [0.54, 0.79]    | 0.584        |
| Fumaric acid                                   | 0.48 [0.22, 0.72]    | 0.37 [0.24, 0.57]    | 0.440        |
| Serine                                         | 5.82 [4.41, 6.94]    | 5.95 [5.18, 7.32]    | 0.531        |
| Threonine                                      | 6.75 [5.98, 8.00]    | 7.37 [6.11, 8.62]    | 0.143        |
| Hydrocinnamic acid                             | 0.12 [0.07, 0.17]    | 0.11 [0.08, 0.16]    | 0.858        |
| Malic acid                                     | 0.14 [0.10, 0.19]    | 0.13 [0.11, 0.16]    | <b>0.048</b> |
| d-Threitol                                     | 0.04 [0.03, 0.06]    | 0.03 [0.03, 0.05]    | <b>0.022</b> |
| Methionine                                     | 1.66 [1.44, 2.17]    | 1.72 [1.54, 2.03]    | 0.252        |
| Oxoproline                                     | 62.55 [50.28, 69.05] | 52.12 [47.24, 70.23] | 0.163        |
| 4-Hydroxyproline                               | 1.91 [1.58, 2.68]    | 2.09 [1.45, 3.21]    | 0.335        |
| Threonic acid                                  | 2.40 [1.84, 4.07]    | 2.37 [1.97, 3.53]    | 1.000        |
| Erythronic acid                                | 0.13 [0.09, 0.26]    | 0.15 [0.09, 0.22]    | 0.771        |
| DL-2-Hydroxyglutaric acid                      | 0.06 [0.05, 0.08]    | 0.06 [0.05, 0.07]    | 0.639        |
| α-ketoglutaric acid                            | 0.75 [0.59, 0.87]    | 0.68 [0.55, 0.87]    | 0.084        |
| Glutamic acid                                  | 5.94 [4.29, 7.36]    | 5.33 [4.12, 6.95]    | 0.185        |
| 4-Hydroxybenzoic acid                          | 0.03 [0.03, 0.04]    | 0.03 [0.02, 0.04]    | 0.069        |
| Phenylalanine                                  | 6.72 [5.89, 8.17]    | 6.82 [5.92, 7.49]    | 0.453        |
| Dodecanoic acid                                | 0.25 [0.16, 0.34]    | 0.22 [0.17, 0.31]    | 0.849        |
| d-Xylose                                       | 0.06 [0.04, 0.09]    | 0.05 [0.03, 0.07]    | 0.181        |
| Taurine                                        | 1.10 [0.77, 1.52]    | 0.92 [0.69, 1.25]    | <b>0.009</b> |
| d-Arabinose                                    | 0.15 [0.10, 0.24]    | 0.12 [0.09, 0.17]    | <b>0.006</b> |
| d-Xylitol                                      | 0.00 [0.00, 0.00]    | 0.00 [0.00, 0.00]    | <b>0.045</b> |
| d-Arabitol                                     | 0.02 [0.02, 0.03]    | 0.02 [0.02, 0.04]    | 0.823        |
| Glycerol-1-phosphate                           | 0.07 [0.06, 0.09]    | 0.08 [0.06, 0.09]    | 0.071        |
| Glutamine                                      | 37.53 [23.67, 43.96] | 35.99 [24.35, 43.01] | 0.128        |
| Xylonic acid                                   | 0.08 [0.05, 0.12]    | 0.09 [0.05, 0.12]    | 0.341        |
| Ribonic acid                                   | 0.02 [0.01, 0.05]    | 0.02 [0.02, 0.04]    | 0.866        |
| 3-Phosphoglyceric acid                         | 0.03 [0.02, 0.05]    | 0.02 [0.02, 0.03]    | <b>0.014</b> |

|                            |                        |                       |              |
|----------------------------|------------------------|-----------------------|--------------|
| Ornithine                  | 18.54 [16.25, 25.32]   | 17.31 [13.80, 22.48]  | <b>0.007</b> |
| Citric acid                | 100.70 [68.09, 138.61] | 85.88 [69.23, 136.88] | 0.488        |
| Tetradecanoic acid         | 1.03 [0.74, 1.45]      | 0.94 [0.77, 1.33]     | 0.663        |
| Hippuric acid              | 1.05 [0.61, 2.12]      | 1.35 [0.50, 2.67]     | 0.297        |
| Vanillylmandelic acid      | 0.03 [0.02, 0.05]      | 0.03 [0.02, 0.04]     | 0.938        |
| 4-hydroxyPhenyllactic acid | 2.41 [1.93, 3.76]      | 2.42 [1.72, 3.31]     | 0.352        |
| d-Fructose                 | 0.04 [0.03, 0.09]      | 0.03 [0.03, 0.08]     | 0.225        |
| d-Mannitol                 | 0.16 [0.09, 0.55]      | 0.16 [0.07, 0.59]     | 0.884        |
| d-Mannonic acid            | 0.17 [0.10, 0.28]      | 0.17 [0.11, 0.30]     | 0.704        |
| d-Galactitol               | 0.02 [0.02, 0.03]      | 0.02 [0.01, 0.03]     | 0.192        |
| Galacturonic acid          | 0.08 [0.05, 0.11]      | 0.07 [0.06, 0.12]     | 0.893        |
| Galactonic acid            | 0.01 [0.00, 0.02]      | 0.01 [0.00, 0.02]     | 0.623        |
| Saccharic acid             | 0.10 [0.06, 0.17]      | 0.10 [0.07, 0.18]     | 0.248        |
| Indole-3-propanoic acid    | 0.06 [0.03, 0.10]      | 0.06 [0.04, 0.09]     | 0.407        |
| Myo-Inositol               | 0.89 [0.73, 1.19]      | 0.79 [0.61, 1.14]     | 0.276        |
| Uric acid                  | 12.55 [8.16, 15.79]    | 11.77 [10.17, 15.28]  | 0.576        |
| Sedoheptulose              | 0.08 [0.06, 0.09]      | 0.07 [0.04, 0.10]     | <b>0.024</b> |
| Indolelactic acid          | 0.53 [0.45, 0.68]      | 0.49 [0.38, 0.74]     | 0.540        |
| Linoleic acid              | 1.68 [1.09, 2.84]      | 1.91 [1.18, 2.70]     | 0.427        |
| Oleic acid                 | 11.53 [5.67, 20.14]    | 12.17 [7.40, 17.05]   | 0.553        |
| Glucose 6-phosphate        | 0.01 [0.00, 0.01]      | 0.01 [0.00, 0.01]     | 0.240        |
| d-Sucrose                  | 0.07 [0.02, 0.17]      | 0.05 [0.02, 0.13]     | 0.313        |
| Maltose                    | 0.05 [0.03, 0.12]      | 0.04 [0.02, 0.07]     | <b>0.003</b> |
| a-Tocopherol               | 0.43 [0.26, 0.62]      | 0.48 [0.29, 0.69]     | <b>0.029</b> |

Results are presented in Relative Units (RU) and displayed as medians [interquartile ranges]. Statistical differences were assessed using the Wilcoxon signed rank test on the log10 RU. SBRT: Stereotactic Ablative Radiation Therapy.

**Table S3.** Plasma metabolite profiles of non-small cell lung cancer (NSCLC) patients pre- and post- CFRT.

|                                                | Pre - CFRT           | Post -CFRT           | p-value      |
|------------------------------------------------|----------------------|----------------------|--------------|
| Plasma metabolites                             | <i>n</i> = 23        | <i>n</i> = 23        |              |
| Pyruvic acid                                   | 8.02 [5.22, 10.28]   | 6.44 [5.39, 8.70]    | 0.709        |
| Lactic acid                                    | 13.87 [12.53, 18.87] | 15.75 [14.12, 19.51] | 0.520        |
| 2-Hydroxyisobutyric acid                       | 0.38 [0.35, 0.49]    | 0.43 [0.32, 0.52]    | 0.393        |
| Glycolic acid                                  | 0.19 [0.16, 0.23]    | 0.18 [0.17, 0.23]    | 0.560        |
| Alanine                                        | 3.02 [2.52, 3.37]    | 3.52 [3.08, 3.68]    | 0.111        |
| 2-Hydroxybutyric acid                          | 4.02 [2.58, 5.54]    | 3.89 [3.05, 5.15]    | 0.754        |
| 3-methyl-2-oxobutyric acid                     | 0.11 [0.09, 0.14]    | 0.11 [0.08, 0.13]    | 0.893        |
| 3-hydroxybutyric acid/3-hydroxyisobutyric acid | 1.41 [0.85, 2.72]    | 1.71 [0.80, 2.56]    | 0.731        |
| 2-Hydroxyisovaleric acid                       | 1.17 [1.06, 2.32]    | 1.44 [1.03, 1.80]    | 0.377        |
| 2-keto-3-methylvaleric acid                    | 0.25 [0.16, 0.29]    | 0.25 [0.20, 0.34]    | 0.119        |
| 3-Hydroxyisovaleric acid                       | 0.24 [0.20, 0.30]    | 0.25 [0.22, 0.30]    | 0.800        |
| Valine                                         | 16.11 [13.51, 20.49] | 17.48 [14.35, 19.98] | 0.540        |
| Benzoic acid                                   | 0.21 [0.18, 0.25]    | 0.19 [0.16, 0.23]    | 0.377        |
| Ethanolamine                                   | 0.27 [0.25, 0.32]    | 0.27 [0.24, 0.32]    | 0.329        |
| Leucine                                        | 7.44 [6.60, 11.02]   | 8.75 [7.78, 11.34]   | 0.126        |
| Phosphoric acid                                | 4.11 [3.01, 4.79]    | 4.42 [3.52, 5.27]    | 0.111        |
| Glycerol                                       | 0.51 [0.38, 0.81]    | 0.51 [0.37, 0.84]    | 0.893        |
| Ethylmalonic acid                              | 0.92 [0.69, 1.20]    | 0.87 [0.71, 1.24]    | 0.917        |
| Isoleucine                                     | 4.25 [3.88, 5.68]    | 5.16 [4.77, 6.49]    | <b>0.023</b> |
| Proline                                        | 30.04 [23.39, 34.46] | 32.01 [23.99, 39.55] | 0.520        |
| Glycine                                        | 1.19 [1.12, 1.32]    | 1.30 [1.20, 1.42]    | <b>0.004</b> |
| Succinic acid                                  | 0.10 [0.08, 0.11]    | 0.09 [0.08, 0.11]    | 0.445        |
| Glyceric acid                                  | 0.78 [0.52, 1.03]    | 0.65 [0.54, 0.89]    | 0.988        |
| Fumaric acid                                   | 0.46 [0.30, 0.58]    | 0.57 [0.39, 0.94]    | <b>0.045</b> |
| Serine                                         | 6.57 [5.00, 7.48]    | 7.30 [6.24, 8.29]    | <b>0.007</b> |
| Threonine                                      | 6.71 [5.48, 7.60]    | 7.30 [6.47, 8.93]    | 0.061        |
| Hydrocinnamic acid                             | 0.09 [0.04, 0.17]    | 0.08 [0.05, 0.11]    | 0.377        |
| Malic acid                                     | 0.11 [0.09, 0.15]    | 0.12 [0.08, 0.17]    | 0.964        |
| d-Threitol                                     | 0.03 [0.03, 0.04]    | 0.03 [0.02, 0.04]    | 0.463        |
| Methionine                                     | 1.45 [1.26, 1.70]    | 1.77 [1.45, 2.05]    | <b>0.011</b> |
| Oxoproline                                     | 53.20 [45.73, 65.12] | 49.38 [44.43, 59.26] | 0.427        |
| 4-Hydroxyproline                               | 1.60 [1.18, 1.80]    | 1.89 [1.27, 2.87]    | 0.151        |
| Threonic acid                                  | 2.64 [2.16, 3.13]    | 2.96 [2.23, 3.78]    | 0.179        |
| Erythronic acid                                | 0.07 [0.06, 0.09]    | 0.07 [0.06, 0.09]    | 0.709        |
| DL-2-Hydroxyglutaric acid                      | 0.05 [0.04, 0.06]    | 0.05 [0.04, 0.06]    | 0.360        |
| α-ketoglutaric acid                            | 0.73 [0.62, 0.93]    | 0.86 [0.78, 1.07]    | <b>0.048</b> |
| Glutamic acid                                  | 9.80 [8.85, 11.61]   | 9.64 [7.46, 13.22]   | 0.463        |
| 4-Hydroxybenzoic acid                          | 0.04 [0.03, 0.05]    | 0.03 [0.02, 0.04]    | 0.134        |
| Phenylalanine                                  | 6.48 [5.41, 7.38]    | 6.85 [5.91, 7.99]    | 0.080        |
| Dodecanoic acid                                | 0.23 [0.18, 0.26]    | 0.19 [0.16, 0.26]    | 0.540        |
| d-Xylose                                       | 0.04 [0.03, 0.06]    | 0.04 [0.03, 0.06]    | 0.974        |
| Taurine                                        | 1.49 [1.12, 1.69]    | 1.27 [0.85, 1.63]    | 0.111        |
| d-Arabinose                                    | 0.15 [0.11, 0.18]    | 0.12 [0.08, 0.19]    | 0.160        |
| d-Xylitol                                      | 0.00 [0.00, 0.00]    | 0.00 [0.00, 0.00]    | 0.465        |
| d-Arabitol                                     | 0.02 [0.02, 0.03]    | 0.02 [0.02, 0.03]    | 0.893        |
| Glycerol-1-phosphate                           | 0.06 [0.05, 0.07]    | 0.06 [0.05, 0.07]    | 0.501        |
| Glutamine                                      | 23.29 [14.34, 28.37] | 27.46 [17.09, 36.59] | 0.151        |
| Xylonic acid                                   | 0.03 [0.03, 0.05]    | 0.04 [0.03, 0.05]    | 0.709        |
| Ribonic acid                                   | 0.01 [0.01, 0.02]    | 0.01 [0.01, 0.02]    | 0.823        |
| 3-Phosphoglyceric acid                         | 0.04 [0.03, 0.05]    | 0.04 [0.03, 0.06]    | 0.284        |

|                            |                       |                        |              |
|----------------------------|-----------------------|------------------------|--------------|
| Ornithine                  | 14.43 [12.52, 17.51]  | 17.37 [13.03, 22.16]   | 0.427        |
| Citric acid                | 97.40 [68.36, 123.65] | 105.55 [70.49, 148.37] | 0.234        |
| Tetradecanoic acid         | 1.00 [0.81, 1.12]     | 0.79 [0.74, 1.17]      | 0.731        |
| Hippuric acid              | 0.81 [0.12, 1.40]     | 0.62 [0.06, 1.58]      | 0.754        |
| Vanillylmandelic acid      | 0.02 [0.02, 0.03]     | 0.02 [0.02, 0.03]      | 0.687        |
| 4-hydroxyPhenyllactic acid | 2.28 [1.86, 2.87]     | 2.22 [1.90, 3.15]      | 0.223        |
| d-Fructose                 | 0.05 [0.04, 0.17]     | 0.05 [0.03, 0.12]      | 0.871        |
| d-Mannitol                 | 0.08 [0.05, 0.30]     | 0.05 [0.04, 0.08]      | 0.065        |
| d-Mannonic acid            | 0.12 [0.10, 0.20]     | 0.11 [0.08, 0.23]      | 0.643        |
| d-Galactitol               | 0.02 [0.02, 0.03]     | 0.03 [0.02, 0.03]      | 0.673        |
| Galacturonic acid          | 0.07 [0.06, 0.09]     | 0.06 [0.04, 0.08]      | 0.329        |
| Galactonic acid            | 0.01 [0.00, 0.02]     | 0.01 [0.00, 0.01]      | 0.665        |
| Saccharic acid             | 0.06 [0.04, 0.08]     | 0.05 [0.04, 0.07]      | 0.345        |
| Indole-3-propanoic acid    | 0.05 [0.03, 0.09]     | 0.05 [0.04, 0.09]      | 0.846        |
| Myo-Inositol               | 0.95 [0.69, 1.06]     | 0.83 [0.68, 1.02]      | 0.665        |
| Uric acid                  | 9.96 [6.60, 19.11]    | 8.98 [4.79, 20.50]     | 0.520        |
| Sedoheptulose              | 0.05 [0.04, 0.07]     | 0.05 [0.04, 0.06]      | 0.200        |
| Indolelactic acid          | 0.46 [0.32, 0.62]     | 0.37 [0.29, 0.47]      | 0.061        |
| Linoleic acid              | 0.93 [0.63, 1.55]     | 1.04 [0.69, 1.96]      | 0.731        |
| Oleic acid                 | 8.05 [4.04, 11.33]    | 9.58 [4.69, 14.85]     | 0.777        |
| Glucose 6-phosphate        | 0.01 [0.01, 0.01]     | 0.01 [0.01, 0.01]      | 0.846        |
| d-Sucrose                  | 0.09 [0.05, 0.13]     | 0.08 [0.04, 0.13]      | 0.870        |
| Maltose                    | 0.22 [0.13, 0.24]     | 0.13 [0.10, 0.19]      | <b>0.028</b> |
| a-Tocopherol               | 0.39 [0.27, 0.43]     | 0.40 [0.24, 0.60]      | 0.893        |

Results are presented in Relative Units (RU) and displayed as medians [interquartile ranges]. Statistical differences were assessed using the Wilcoxon signed rank test on the log<sub>10</sub> RU. CFRT: Conventionally Fractionated Radiation Therapy.