

# Health-related quality of life of patients with brain metastases selected for stereotactic radiosurgery

Eline Verhaak<sup>1,2,3</sup>, Karin Gehring<sup>1,2,3</sup>, Patrick E. J. Hanssens<sup>1,2</sup>, AND Margriet M. Sitskoorn<sup>2,3</sup>

<sup>1</sup> Gamma Knife Center, Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands

<sup>2</sup> Department of Neurosurgery, Elisabeth-TweeSteden Hospital, Tilburg, The Netherlands

<sup>3</sup> Department of Cognitive Neuropsychology, Tilburg University, Tilburg, The Netherlands

Corresponding author: Karin Gehring (E-mail: k.gehring@tilburguniversity.edu, Telephone number: +31 13 466 4233)

## Results of the exploratory univariate analyses of predictors of pre-SRS HRQoL of patients with BM – CAR-Study A (NCT02953756)

**Supplementary Table 1.** Univariate analyses of predictors of pre-SRS HRQoL of 92 patients with BM

|                                  |                                | PWB              | SWB                 | EWB              | FWB              | FACT-G            | BRCS              | FACT-Br            | TOI                |
|----------------------------------|--------------------------------|------------------|---------------------|------------------|------------------|-------------------|-------------------|--------------------|--------------------|
| <b>Socio-demographic factors</b> |                                |                  |                     |                  |                  |                   |                   |                    |                    |
| Age                              | b                              | -0.004           | -0.063 <sup>‡</sup> | 0.012            | -0.037           | -0.081            | -0.148            | -0.229             | -0.188             |
|                                  | 95% CI                         | -0.107 to 0.099  | -0.170 to 0.044     | -0.089 to 0.113  | -0.168 to 0.093  | -0.417 to 0.255   | -0.387 to 0.092   | -0.743 to 0.286    | -0.592 to 0.215    |
|                                  | <i>p</i> value                 | .943             | .243                | .811             | .573             | .634              | .224              | .380               | .355               |
|                                  | <i>Adjusted R</i> <sup>2</sup> | -.011            | .004                | -.010            | -.008            | -.009             | .005              | -.002              | -.002              |
| Sex<br>Female vs Male (ref)      | b                              | -0.880           | 1.150               | -1.870           | -0.656           | -2.257            | -1.981            | -4.237             | -3.516             |
|                                  | 95% CI                         | -2.865 to 1.106  | -1.047 to 3.347     | -3.785 to -0.044 | -3.179 to 1.867  | -8.747 to 4.234   | -6.630 to 2.669   | -14.196 to 5.722   | -11.314 to 4.281   |
|                                  | <i>p</i> value                 | .381             | .301                | .055             | .607             | .492              | .400              | .400               | .373               |
|                                  | <i>Adjusted R</i> <sup>2</sup> | -.002            | .001                | .030             | -.008            | -.006             | -.003             | -.003              | -.002              |
| <b>Clinical factors</b>          |                                |                  |                     |                  |                  |                   |                   |                    |                    |
| KPS<br>70 - 80 vs 90 - 100 (ref) | b                              | -3.405           | -2.010              | -1.418           | -4.968           | -11.800           | -9.574            | -21.374            | -17.947            |
|                                  | 95% CI                         | -5.357 to -1.453 | -4.275 to 0.255     | -3.433 to 0.597  | -7.387 to -2.548 | -18.117 to -5.484 | -14.007 to -5.141 | -30.785 to -11.963 | -25.194 to -10.700 |
|                                  | <i>p</i> value                 | <b>.001</b>      | .081                | .166             | <b>&lt;.001</b>  | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>    | <b>&lt;.001</b>    |
|                                  | <i>Adjusted R</i> <sup>2</sup> | .108             | .023                | .010             | .147             | .123              | .161              | .175               | .203               |
| Total BM volume                  | b                              | -0.011           | -0.025              | 0.024            | -0.027           | -0.039            | -0.098            | -0.137             | -0.136             |
|                                  | 95% CI                         | -0.142 to 0.121  | -0.171 to 0.121     | -0.105 to 0.152  | -0.194 to 0.139  | -0.468 to 0.390   | -0.405 to 0.209   | -0.796 to 0.522    | -0.652 to 0.380    |
|                                  | <i>p</i> value                 | .873             | .735                | .715             | .748             | .858              | .527              | .680               | .602               |
|                                  | <i>Adjusted R</i> <sup>2</sup> | -.011            | -.010               | -.010            | -.010            | -.011             | -.007             | -.009              | -.008              |
| Seizures<br>Yes vs No (ref)      | b                              | 0.104            | -2.720              | 0.000            | -1.558           | -4.174            | -3.510            | -7.684             | -4.965             |
|                                  | 95% CI                         | -2.233 to 2.440  | -5.247 to -0.193    | -2.290 to 2.290  | -4.502 to 1.385  | -11.750 to 3.402  | -8.931 to 1.911   | -19.291 to 3.922   | -14.085 to 4.155   |
|                                  | <i>p</i> value                 | .930             | <b>.035</b>         | 1.000            | .296             | .277              | .202              | .192               | .282               |
|                                  | <i>Adjusted R</i> <sup>2</sup> | -.011            | .038                | -.011            | .001             | .002              | .007              | .008               | .002               |

|                                 |                                | <b>PWB</b>          | <b>SWB</b>       | <b>EWB</b>       | <b>FWB</b>       | <b>FACT-G</b>     | <b>BRCS</b>       | <b>FACT-Br</b>    | <b>TOI</b>        |
|---------------------------------|--------------------------------|---------------------|------------------|------------------|------------------|-------------------|-------------------|-------------------|-------------------|
| RPA                             | b                              | -3.942              | 0.535            | -0.832           | -2.013           | -6.252            | -3.378            | -9.631            | -9.333            |
| Class 1 vs Class 2 (ref)        | 95% CI                         | -6.439 to -1.445    | -2.378 to 3.448  | -3.404 to 1.739  | -5.319 to 1.293  | -14.734 to 2.230  | -9.494 to 2.737   | -22.662 to 3.401  | -19.477 to 0.810  |
|                                 | <i>p</i> value                 | <b>.002</b>         | .716             | .522             | .230             | .147              | .275              | .146              | .071              |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .089                | -.010            | -.006            | .005             | .012              | .002              | .013              | .025              |
| GPA                             | b                              | 0.824               | 2.129            | 2.294            | 3.537            | 8.784             | 0.245             | 9.029             | 4.606             |
| Class 2 vs Class 4 (ref)        | 95% CI                         | -2.569 to 4.217     | -1.620 to 5.877  | -1.007 to 5.595  | -0.712 to 7.787  | -2.176 to 19.744  | -7.729 to 8.219   | -7.943 to 26.002  | -8.732 to 17.945  |
| Class 3 vs Class 4 (ref)        | b                              | -0.315              | 1.207            | 1.411            | 1.237            | 3.540             | 0.030             | 3.570             | 0.953             |
|                                 | 95% CI                         | -2.947 to 2.317     | -1.701 to 4.114  | -1.150 to 3.971  | -2.059 to 4.533  | -4.961 to 12.040  | -6.154 to 6.215   | -9.594 to 16.734  | -9.393 to 11.298  |
|                                 | <i>p</i> value                 | .715                | .523             | .370             | .248             | .282              | .998              | .570              | .758              |
|                                 | <i>Adjusted R</i> <sup>2</sup> | -.015               | -.008            | .000             | .009             | .006              | -.022             | -.010             | -.016             |
| Symptomatic BM                  | b                              | -0.081              | -0.918           | -0.051           | -1.614           | -2.664            | -3.676            | -6.339            | -5.370            |
| Yes vs No (ref)                 | 95% CI                         | -2.247 to 2.085     | -3.311 to 1.476  | -2.174 to 2.072  | -4.338 to 1.111  | -9.711 to 4.384   | -8.688 to 1.337   | -17.120 to 4.442  | -13.805 to 3.064  |
|                                 | <i>p</i> value                 | .941                | .448             | .962             | .242             | .455              | .149              | .246              | .209              |
|                                 | <i>Adjusted R</i> <sup>2</sup> | -.011               | -.005            | -.011            | .004             | -.005             | .012              | .004              | .007              |
| Illness duration                | b                              | -0.028              | -0.008           | 0.001            | -0.015           | -0.050            | -0.014            | -0.065            | -0.058            |
|                                 | 95% CI                         | -0.056 to 0.000     | -0.040 to 0.024  | -0.027 to 0.029  | -0.051 to 0.021  | -0.143 to 0.043   | -0.081 to 0.053   | -0.208 to 0.079   | -0.170 to 0.054   |
|                                 | <i>p</i> value <sup>a</sup>    | <b>.048</b>         | .619             | .948             | .411             | .285              | .676              | .373              | .310              |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .032                | -.008            | -.011            | -.003            | .002              | -.009             | -.002             | .000              |
| Diagnosis of BM                 | b                              | -2.947              | -2.932           | 0.051            | -1.871           | -7.698            | -6.807            | -14.506           | -11.625           |
| Metachronous vs                 | 95% CI                         | -5.024 to -0.871    | -5.253 to -0.610 | -2.072 to 2.174  | -4.588 to 0.847  | -14.582 to -0.815 | -11.674 to -1.941 | -24.935 to -4.077 | -19.779 to -3.471 |
| Synchronous (ref)               | <i>p</i> value                 | <b>.006</b>         | <b>.014</b>      | .962             | .175             | <b>.029</b>       | <b>.007</b>       | <b>.007</b>       | <b>.006</b>       |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .071                | .055             | -.011            | .009             | .041              | .069              | .068              | .072              |
| <b>Psychological factors</b>    |                                |                     |                  |                  |                  |                   |                   |                   |                   |
| General Fatigue                 | b                              | -0.705 <sup>‡</sup> | -0.216           | -0.390           | -0.822           | -2.094            | -1.114            | -3.208            | -2.602            |
|                                 | 95% CI                         | -0.861 to -0.549    | -0.469 to 0.037  | -0.602 to -0.178 | -1.061 to -0.584 | -2.712 to -1.476  | -1.605 to -0.623  | -4.159 to -2.257  | -3.334 to -1.871  |
|                                 | <i>p</i> value                 | <b>&lt;.001</b>     | .094             | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .466                | .020             | .119             | .335             | .327              | .175              | .325              | .350              |
| Physical Fatigue                | b                              | -0.660              | -0.196           | -0.377           | -0.787           | -2.020            | -1.167            | -3.188            | -2.615            |
|                                 | 95% CI                         | -0.826 to -0.494    | -0.432 to 0.040  | -0.574 to -0.181 | -1.006 to -0.568 | -2.585 to -1.456  | -1.610 to -0.724  | -4.042 to -2.334  | -3.263 to -1.966  |
|                                 | <i>p</i> value                 | <b>&lt;.001</b>     | .102             | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .402                | .019             | .129             | .355             | .353              | .225              | .373              | .409              |
| Reduced Activity                | b                              | -0.652              | -0.334           | -0.468           | -0.934           | -2.388            | -1.396            | -3.784            | -2.982            |
|                                 | 95% CI                         | -0.859 to -0.445    | -0.599 to -0.068 | -0.691 to -0.246 | -1.180 to -0.688 | -3.024 to -1.753  | -1.897 to -0.895  | -4.741 to -2.827  | -3.729 to -2.235  |
|                                 | <i>p</i> value                 | <b>&lt;.001</b>     | <b>.014</b>      | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .296                | .054             | .154             | .381             | .376              | .246              | .400              | .405              |
| Reduced Motivation <sup>a</sup> | b                              | -0.643              | -0.384           | -0.506           | -0.967           | -2.501            | -1.372            | -3.873            | -2.982            |
|                                 | 95% CI                         | -0.874 to -0.412    | -0.670 to -0.098 | -0.745 to -0.268 | -1.238 to -0.696 | -3.197 to -1.805  | -1.930 to -0.814  | -4.941 to -2.805  | -3.828 to -2.137  |
|                                 | <i>p</i> value                 | <b>&lt;.001</b>     | <b>.009</b>      | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   | <b>&lt;.001</b>   |
|                                 | <i>Adjusted R</i> <sup>2</sup> | .248                | .064             | .157             | .353             | .357              | .203              | .361              | .348              |

|   |                         | <b>PWB</b>          | <b>SWB</b>         | <b>EWB</b>       | <b>FWB</b>       | <b>FACT-G</b>    | <b>BRCS</b>      | <b>FACT-Br</b>   | <b>TOI</b>       |
|---|-------------------------|---------------------|--------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| Mental Fatigue <sup>a</sup>                       | b                       | -0.485              | -0.135             | -0.202           | -0.437           | -1.259           | -1.530           | -2.789           | -2.452           |
|   | 95% CI                  | -0.712 to -0.258    | -0.408 to 0.137    | -0.447 to 0.043  | -0.738 to -0.137 | -2.016 to -0.503 | -2.025 to -1.035 | -3.884 to -1.695 | -3.284 to -1.621 |
|   | p value                 | <b>&lt;.001</b>     | .326               | .105             | <b>.005</b>      | <b>.001</b>      | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  |
|   | Adjusted R <sup>2</sup> | .159                | .000               | .018             | .076             | .099             | .290             | .215             | .270             |
| Anxiety   | b                       | -0.449              | -0.189             | -0.749           | -0.575           | -1.963           | -1.028           | -2.991           | -2.053           |
|   | 95% CI                  | -0.659 to -0.240    | -0.441 to 0.063    | -0.911 to -0.588 | -0.841 to -0.310 | -2.590 to -1.336 | -1.521 to -0.535 | -3.958 to -2.024 | -2.847 to -1.259 |
|   | p value                 | <b>&lt;.001</b>     | .139               | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  |
|   | Adjusted R <sup>2</sup> | .158                | .013               | .480             | .162             | .293             | .151             | .288             | .218             |
| Depression  | b                       | -0.730 <sup>‡</sup> | -0.340             | -0.638           | -0.969           | -2.671           | -1.558           | -4.230           | -3.251           |
|   | 95% CI                  | -0.932 to -0.528    | -0.601 to -0.079   | -0.837 to -0.440 | -1.202 to -0.735 | -3.239 to -2.104 | -2.028 to -1.089 | -5.075 to -3.385 | -3.927 to -2.576 |
|   | p value                 | <b>&lt;.001</b>     | <b>.011</b>        | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  | <b>&lt;.001</b>  |
|   | Adjusted R <sup>2</sup> | .357                | .059               | .305             | .424             | .487             | .319             | .518             | .498             |
| <b>Cognitive factors</b>                          |                         |                     |                    |                  |                  |                  |                  |                  |                  |
| Immediate verbal memory                           | b                       | -0.214              | 0.969 <sup>‡</sup> | -0.355           | 0.305            | 0.631            | 1.007            | 1.639            | 1.098            |
|   | 95% CI                  | -0.930 to 0.502     | 0.432 to 1.505     | -1.054 to 0.344  | -0.602 to 1.211  | -1.705 to 2.968  | -0.658 to 2.672  | -1.940 to 5.218  | -1.709 to 3.905  |
|   | p value                 | .554                | <b>.001</b>        | .316             | .506             | .593             | .233             | .365             | .439             |
|   | Adjusted R <sup>2</sup> | -.007               | .115               | .000             | -.006            | -.008            | .005             | -.002            | -.004            |
| Delayed verbal memory                             | b                       | -0.035              | 0.724 <sup>‡</sup> | -0.388           | 0.259            | 0.322            | 1.277            | 1.599            | 1.501            |
|   | 95% CI                  | -0.823 to 0.752     | -0.169 to 1.617    | -1.155 to 0.380  | -0.737 to 1.256  | -2.247 to 2.890  | -0.547 to 3.101  | -2.336 to 5.533  | -1.576 to 4.578  |
|   | p value                 | .929                | .111               | .318             | .607             | .804             | .168             | .422             | .335             |
|   | Adjusted R <sup>2</sup> | -.011               | .017               | .000             | -.008            | -.010            | .010             | -.004            | -.001            |
| Executive functioning <sup>b</sup>                | b                       | -0.059              | 0.126              | -0.147           | -0.104           | -0.185           | 0.175            | -0.010           | 0.012            |
|   | 95% CI                  | -0.505 to 0.386     | -0.363 to 0.615    | -0.557 to 0.262  | -0.657 to 0.449  | -1.607 to 1.237  | -0.842 to 1.193  | -2.200 to 2.180  | -1.711 to 1.735  |
|   | p value                 | .791                | .610               | .477             | .709             | .796             | .733             | .993             | .989             |
|   | Adjusted R <sup>2</sup> | -.012               | -.009              | -.006            | -.011            | -.012            | -.011            | -.013            | -.013            |
| Motor dexterity<br>Dominant hand <sup>c</sup>     | b                       | 0.098               | 0.320              | 0.250            | 0.279            | 0.947            | 1.275            | 2.222            | 1.652            |
|   | 95% CI                  | -0.268 to 0.463     | -0.082 to 0.721    | -0.089 to 0.589  | -0.176 to 0.734  | -0.222 to 2.116  | 0.465 to 2.085   | 0.461 to 3.982   | 0.266 to 3.037   |
|   | p value                 | .596                | .117               | .146             | .226             | .111             | <b>.002</b>      | <b>.014</b>      | <b>.020</b>      |
|   | Adjusted R <sup>2</sup> | -.008               | .017               | .013             | .006             | .018             | .092             | .057             | .050             |
| Motor dexterity<br>Non-dominant hand <sup>c</sup> | b                       | 0.108               | 0.474              | 0.059            | 0.380            | 1.021            | 1.383            | 2.404            | 1.871            |
|   | 95% CI                  | -0.364 to 0.580     | -0.041 to 0.989    | -0.404 to 0.523  | -0.202 to 0.961  | -0.489 to 2.531  | 0.333 to 2.434   | 0.123 to 4.685   | 0.089 to 3.653   |
|   | p value                 | .650                | .071               | .800             | .198             | .183             | <b>.010</b>      | <b>.039</b>      | <b>.040</b>      |
|   | Adjusted R <sup>2</sup> | -.009               | .026               | -.011            | .008             | .009             | .063             | .038             | .037             |

Note: <sup>‡</sup> Weighted Least Squares regression, <sup>a</sup> n=91, <sup>b</sup> n=80, <sup>c</sup> n=88

BM: brain metastases, BRCS: brain cancer subscale, CI: confidence interval, EWB: Emotional well-being, FACT-Br: Functional Assessment of Cancer Therapy-Brain, FACT-G: FACT-General, FWB: Functional well-being, GPA: Graded Prognostic Assessment, HRQoL: Health-related quality of life, KPS: Karnofsky performance status, PWB: Physical well-being, ref: reference category, RPA: Recursive Partitioning Analysis, SWB: Social well-being, TOI: trial outcome index, vs: versus