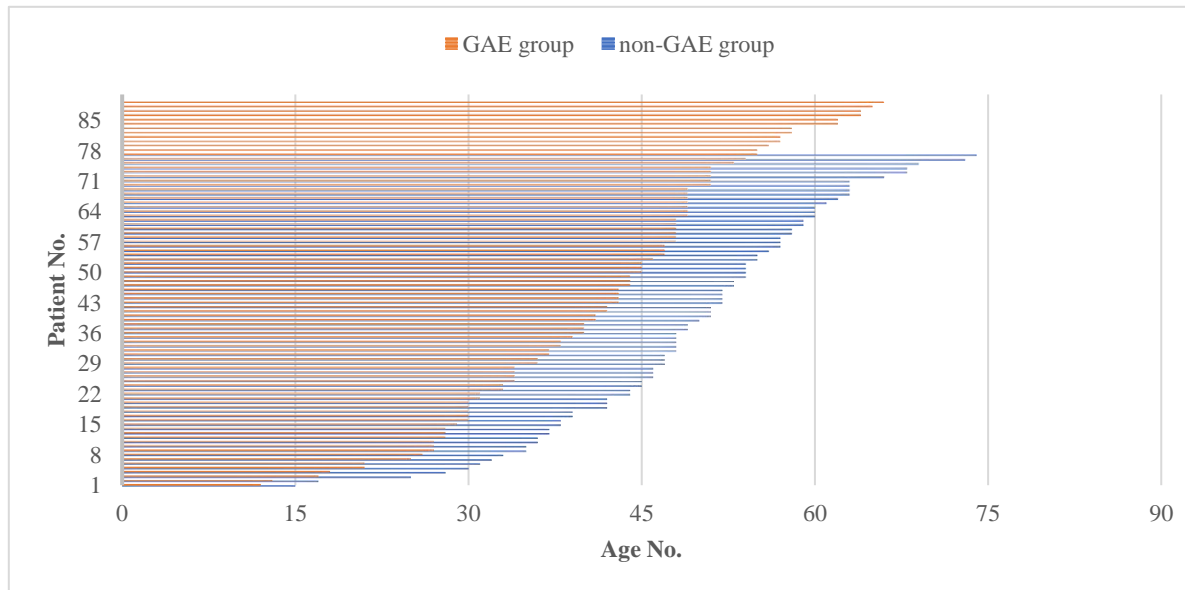


**Appendix 1a.** The glioma sub-types in cohort of all patients.

| Group           | WHO grade II (n=78) |  | WHO grade III (n=35) |  | WHO grade IV (n=53) |                  | All cohort       |                  |
|-----------------|---------------------|--|----------------------|--|---------------------|------------------|------------------|------------------|
|                 | IDH <sub>w</sub>    | IDH <sub>M</sub> (1p19q non-codel/1p19q codel/1p19q unknown) | IDH <sub>w</sub>     | IDH <sub>M</sub> (1p19q non-codel/1p19q codel/1p19q unknown) | IDH <sub>w</sub>    | IDH <sub>M</sub> | IDH <sub>w</sub> | IDH <sub>M</sub> |
| GAE group       | 3                   | 53 (7/28/18)   | 3                    | 16 (1/10/5)  | 11                  | 3                | 17               | 72               |
| Non-GAE group   | 3                   | 19 (11/5/3)  | 1                    | 15 (0/13/2)  | 35                  | 4                | 39               | 38               |
| Age (mean ± SD) | -                   | -  | -                    | -  | -                   | -                | 50.5±14.1        | 42.3±10.9        |

**Note.** IDH<sub>w</sub>, isocitrate dehydrogenase wild type. IDH<sub>M</sub>, isocitrate dehydrogenase mutation type. 1p19q non-codel/1p19q codel/1p19q unknown, 1p19q non-codeletion/1p19q codeletions/1p19q has no pathology result.

**Appendix 1b.** The age distribution of all patients.



**Appendix 2. Features selected in models.**

| Model                      | Feature number | Individual features                                 | Feature contribution<br>(P or N) |
|----------------------------|----------------|---|----------------------------------|
| Shape model                | 5              | Maximum 3D diameter                                 | 4.043638915 (P)                  |
|                            |                | Flatness  | -4.771486845 (N)                 |
|                            |                | Maximum 2D diameter column                          | 5.128985868 (P)                  |
|                            |                | Maximum 2D diameter slice                           | -6.839350673 (N)                 |
|                            |                | Major axis length                                   | -7.554585705 (N)                 |
| Original first order model | 4              | Mean  | -3.453293469 (N)                 |
|                            |                | 90 Percentile                                       | -4.983274637 (N)                 |
|                            |                | Total energy  | -23.529752261 (N)                |
|                            |                | Energy  | 23.888512103 (P)                 |
| Original texture model     | 5              | GLDM large dependence low grade gray level emphasis | /                                |
|                            |                | GLCM cluster shade                                  | /                                |
|                            |                | GLDM high gray level emphasis                       | /                                |
|                            |                | GLRLM long run high gray level emphasis             | /                                |
|                            |                | GLSZM size zone nonuniformity normalized            | /                                |
| LoG first order model      | 10             | 5.0 mm variance                                     | 1.711433659 (P)                  |
|                            |                | 1.0 mm variance                                     | -2.565389036 (N)                 |
|                            |                | 3.0 mm variance                                     | 3.480931693 (P)                  |
|                            |                | 5.0 kurtosis  | 5.131740485 (P)                  |
|                            |                | 1.0 mm Interquartile range                          | -5.672505266 (N)                 |
|                            |                | 3.0 mm total energy                                 | -7.025115512 (N)                 |
|                            |                | 1.0 mm total energy                                 | -7.673385179 (N)                 |
|                            |                | 1.0 mm energy                                       | 9.899469043 (P)                  |
|                            |                | 5.0 mm total energy                                 | -10.310174754 (N)                |
|                            |                | 3.0 mm energy                                       | 11.859891052 (P)                 |
| LoG texture model          | 3              | 1.0mm 3D GLSZM small area emphasis                  | /                                |
|                            |                | 5.0mm 3D GLDM dependence nonuniformity normalized   | /                                |

|                                  |    |   |                  |
|----------------------------------|----|---|------------------|
|                                  |    | 3.0mm 3D GLDM dependence nonuniformity normalized         | /                |
| Wavelet first order model        | 3  | HHL kurtosis  | /                |
|                                  |    | HHL root mean squared                                     | /                |
|                                  |    | HHL 10 percentile   | /                |
| Wavelet texture model            | 5  | HHL GLDM low gray level emphasis                          | 4.606567694 (P)  |
|                                  |    | HHL GLDM large dependence low gray level emphasis         | 4.648666650 (P)  |
|                                  |    | LHL GLCM correlation                                      | 9.817323275 (P)  |
|                                  |    | HHL GLCM correlation                                      | 11.179233591 (P) |
|                                  |    | LHL GLRLM run variance                                    | 16.401634450 (P) |
| Clinical model                   | 3  | Gender  | -2.216162957 (N) |
|                                  |    | Age   | -2.576434188 (N) |
|                                  |    | Pathological grade  | -3.726135869 (N) |
| Radiomic features combined model | 14 | Original first order 90 percentile                        | -0.098420960 (N) |
|                                  |    | Original first order mean                                 | 0.157985654 (P)  |
|                                  |    | Wavelet HHL first order root mean squared                 | -0.237031026 (N) |
|                                  |    | LoG 1.0mm 3D GLSZM small area emphasis                    | -0.350729256 (N) |
|                                  |    | Wavelet HHL GLDM low gray level emphasis                  | 0.355376817 (P)  |
|                                  |    | LoG 3.0mm 3D GLDM dependence non-uniformity normalized    | 0.401618639 (P)  |
|                                  |    | Wavelet HHL GLDM large dependence low gray level emphasis | 0.444118604 (P)  |
|                                  |    | Wavelet HHL first order 10 percentile                     | 0.554403570 (P)  |
|                                  |    | Wavelet LHL GLRLM run variance                            | 0.763101889 (P)  |
|                                  |    | Original GLSZM size zone non-uniformity normalized        | -0.764766468 (N) |
|                                  |    | LoG 5.0mm 3D GLDM dependence non-uniformity normalized    | 0.876333725 (P)  |
|                                  |    | Wavelet HHL GLCM correlation                              | 0.885652900 (P)  |
|                                  |    | Wavelet LHL GLCM correlation                              | 0.968529651 (P)  |
|                                  |    | Wavelet HHL first order kurtosis                          | 1.084351551 (P)  |
| Clinic-radiomic model            | 19 | The same with Table 3.                                    |                  |

**Note.** P or N, shortly for positive and negative correlation in model. GLCM, Gray-Level Co-occurrence Matrix; GLDM, Gray Level Dependence Matrix; GLRLM, Gray Level Run Length Matrix; GLSZM, Gray-Level Size Zone Matrix. "/" indicates that the model used random forest as a classifier, so there was no definite contribution of features.

### **Appendix 3.**

All features were normalized before feature selection. To reduce their dimension and select the appropriate ones for radiomics model building, we used a heuristic approach. First, features were divided into sub-groups according to their category, such as first-order, shape and texture, and a scout model was built with those features for each subgroup, using the training dataset. The scout models were evaluated with a 10-fold cross-validation, and when the average cross-validation area under the receiver operating characteristic curve (AUC) was  $> 0.6$ , all features in the model were retained for final model building. Otherwise, no subgroup features were further used.”

For example, 14 shape features formed a subgroup. In this group, 9 different models pipelines (3x3) were built and compared performed as we described before.

Appendix 4 and 5 list the first five models sorted by their performance on cross-validation cohort. Since the optimalbest scout model obtained an AUC of 0.647 which was smaller than 0.7, shape features were not used for establishing radiomics signature and clinic-radiomic model. Conversely, for the subgroup of first-order features in original images, the optimalbest scout model achieved an AUC of 0.758 on cross-validation set, so 4 features retained in this model were selected for the building of radiomics models further trail. In this way, redundant features were reduced, which was helpful to find candidate model with all categories of features. It is worth noof noteing that the process of feature selection was only performedonly carried on training cohort via cross-validation, so without leaking information leaking of testing cohort was avoided.

**Appendix 4. The first five models in each subgroup ordered by their AUC on cross-validation cohort. Model named by its feature selector method, classifier and the feature number it used.**

| <b>Scout model</b>   | <b>Model name</b> | <b>AUC on cross-validation cohort</b> |
|----------------------|-------------------|---------------------------------------|
| Shape                | Relief-LR-5       | 0.647                                 |
|                      | RFE-LR-2          | 0.646                                 |
|                      | RFE-LR-3          | 0.642                                 |
|                      | RFE-LR-5          | 0.641                                 |
|                      | RFE-LR-4          | 0.641                                 |
| Original first-order | Relief-LR-4       | 0.738                                 |
|                      | Relief-LR-10      | 0.737                                 |
|                      | Relief-LR-5       | 0.736                                 |
|                      | Relief-LR-6       | 0.734                                 |
|                      | Relief-LR-11      | 0.723                                 |
| Original texture     | Relief-RF-5       | 0.784                                 |
|                      | KW-LR-19          | 0.783                                 |
|                      | KW-LR-20          | 0.782                                 |
|                      | KW-LR-18          | 0.781                                 |
|                      | Relief-RF-22      | 0.780                                 |
| Wavelet first-order  | RFE-RF-3          | 0.831                                 |
|                      | RFE-LR-15         | 0.826                                 |
|                      | RFE-LR-9          | 0.823                                 |
|                      | RFE-LR-12         | 0.822                                 |
|                      | RFE-LR-14         | 0.821                                 |
| Wavelet texture      | RFE-LR-5          | 0.828                                 |
|                      | RFE-SVM-4         | 0.824                                 |
|                      | RFE-LR-4          | 0.822                                 |
|                      | RFE-SVM-5         | 0.813                                 |
|                      | Relief-SVM-26     | 0.811                                 |
| LoG first-order      | Relief-LR-10      | 0.786                                 |
|                      | Relief-LR-7       | 0.785                                 |
|                      | Relief-LR-8       | 0.764                                 |
|                      | RFE-LR-16         | 0.761                                 |
|                      | Relief-LR-9       | 0.759                                 |
| LoG texture          | KW-RF-3           | 0.817                                 |
|                      | KW-RF-2           | 0.805                                 |
|                      | RFE-SVM-13        | 0.787                                 |
|                      | KW-RF-13          | 0.783                                 |
|                      | RFE-SVM-14        | 0.782                                 |

**Appendix 5. The performance of scout models in predict GAE in training and testing cohort.**

| Model                            | Cohort           | AUC (95% CI)               | Accuracy | Sensitivity | Specificity | PPV   | NPV   |
|----------------------------------|------------------|----------------------------|----------|-------------|-------------|-------|-------|
| Shape model                      | Training         | 0.684 (0.577-0.785)        | 0.694    | 0.738       | 0.640       | 0.714 | 0.667 |
|                                  | Cross-validation | 0.647 (0.538-0.752)        | 0.658    | 0.607       | 0.720       | 0.736 | 0.600 |
| Original first order model       | Training         | 0.758 (0.664-0.840)        | 0.730    | 0.754       | 0.700       | 0.754 | 0.700 |
|                                  | Cross-validation | 0.738 (0.639-0.831)        | 0.703    | 0.623       | 0.800       | 0.792 | 0.635 |
| Original texture model           | Training         | 0.923(0.868-0.964)         | 0.847    | 0.754       | 0.960       | 0.958 | 0.762 |
|                                  | Cross-validation | 0.784 (0.698-0.868)        | 0.730    | 0.541       | 0.960       | 0.943 | 0.632 |
| LoG first order model            | Training         | 0.786 (0.698-0.867)        | 0.748    | 0.853       | 0.620       | 0.732 | 0.775 |
|                                  | Cross-validation | 0.786 (0.698-0.864)        | 0.730    | 0.639       | 0.840       | 0.830 | 0.656 |
| LoG texture model                | Training         | 0.733 (0.634-0.828)        | 0.757    | 0.574       | 0.980       | 0.972 | 0.653 |
|                                  | Cross-validation | 0.817 (0.736-0.891)        | 0.748    | 0.623       | 0.900       | 0.884 | 0.662 |
| Wavelet first order model        | Training         | 0.781 (0.692-0.865)        | 0.730    | 0.525       | 0.980       | 0.970 | 0.628 |
|                                  | Cross-validation | 0.831 (0.747-0.903)        | 0.793    | 0.754       | 0.840       | 0.852 | 0.737 |
| Wavelet texture model            | Training         | 0.815 (0.729-0.889)        | 0.784    | 0.689       | 0.90        | 0.894 | 0.703 |
|                                  | Cross-validation | 0.828 (0.739-0.897)        | 0.784    | 0.738       | 0.840       | 0.849 | 0.724 |
| Clinical model                   | Training         | 0.762 (0.667-0.846)        | 0.748    | 0.721       | 0.780       | 0.800 | 0.696 |
|                                  | Testing          | 0.799 (0.672-0.917)        | 0.782    | 0.750       | 0.815       | 0.808 | 0.759 |
| Radiomic features combined model | Training         | 0.879 (0.805-0.939)        | 0.811    | 0.770       | 0.86        | 0.870 | 0.754 |
|                                  | Testing          | 0.724 (0.575-0.855)        | 0.673    | 0.536       | 0.815       | 0.750 | 0.629 |
| Clinic-radiomic model            | Training cohort  | 0.886 (0.819-0.940)        | 0.820    | 0.803       | 0.840       | 0.860 | 0.778 |
|                                  | Testing          | <b>0.836 (0.707-0.937)</b> | 0.782    | 0.750       | 0.815       | 0.808 | 0.759 |
| Model                            | Cohort           | AUC (95% CI)               | Accuracy | Sensitivity | Specificity | PPV   | NPV   |
|                                  | Cross-validation | 0.647 (0.538-0.752)        | 0.658    | 0.607       | 0.720       | 0.736 | 0.600 |
| Original first order model       | Training         | 0.758 (0.664-0.840)        | 0.730    | 0.754       | 0.700       | 0.754 | 0.700 |
|                                  | Cross-validation | 0.738 (0.639-0.831)        | 0.703    | 0.623       | 0.800       | 0.792 | 0.635 |
| Original texture                 | Training         | 0.923(0.868-0.964)         | 0.847    | 0.754       | 0.960       | 0.958 | 0.762 |

|                     |                  |                     |       |       |       |       |       |
|---------------------|------------------|---------------------|-------|-------|-------|-------|-------|
| model               | Cross-validation | 0.784 (0.698-0.868) | 0.730 | 0.541 | 0.960 | 0.943 | 0.632 |
| LoG first order     | Training         | 0.786 (0.698-0.867) | 0.748 | 0.853 | 0.620 | 0.732 | 0.775 |
| model               | Cross-validation | 0.786 (0.698-0.864) | 0.730 | 0.639 | 0.840 | 0.830 | 0.656 |
| LoG texture         | Training         | 0.733 (0.634-0.828) | 0.757 | 0.574 | 0.980 | 0.972 | 0.653 |
| model               | Cross-validation | 0.817 (0.736-0.891) | 0.748 | 0.623 | 0.900 | 0.884 | 0.662 |
| Wavelet first order | Training         | 0.781 (0.692-0.865) | 0.730 | 0.525 | 0.980 | 0.970 | 0.628 |
| model               | Cross-validation | 0.831 (0.747-0.903) | 0.793 | 0.754 | 0.840 | 0.852 | 0.737 |
| Wavelet texture     | Training         | 0.815 (0.729-0.889) | 0.784 | 0.689 | 0.90  | 0.894 | 0.703 |
| model               | Cross-validation | 0.828 (0.739-0.897) | 0.784 | 0.738 | 0.840 | 0.849 | 0.724 |