Supplementary Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

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**eMethods 1. Annotation of Tumors in Training Data**

For the precise localization of tumor regions, the tumors were labeled on the MRI scans under the supervision of neuroradiologists. The tumor and cyst areas were annotated using a single binary annotation label. Labeling was done on the T2 axial volume, and T1 contrast-enhanced axial volume.
eMethods 2. Development of Deep Learning System (DLS)

Design and training of the Deep Learning System

To detect and classify 18 different types of tumors, a two-staged deep learning system (DLS) was designed. Stage one of the DLS consisted of a segmentation network that segmented the tumor regions from the healthy tissue and the second stage classified the identified tumor into one of the 18 classes. This complete architecture of the DLS is presented in supplemental figure S2.

Before the processing with the DLS, all the available 3D MRI scans were preprocessed with intensity normalization to have zero mean and unit standard deviation. Next, the scans were spatially normalized with bilinear interpolation to have uniform axial slice dimensions of 256x256 pixels. Considering the high pixel spacing along the axial direction which would result in poor interpolation performance, the images were not interpolated along the axial direction and an original number of axial slices was retained. Also, when using data from multiple MRI sequences, no head alignment, skull stripping, or registration to a standard brain template was performed to avoid the introduction of any potential registration errors and to reduce the processing time.

The first stage of the DLS was designed as a modified 2D U-Net architecture that performed a binary segmentation of tumor regions from the 2D axial slices of the preprocessed MRI sequences. The complete 3D tumor segmentation was obtained by concatenating the 2D predictions from all axial slices. As presented in supplemental figure S2, the modified UNet architecture used in this work consisted of 4 down-sampling and corresponding 4-up-sampling convolution blocks. This stage of the DLS was trained with 30% of the training data (N = 11,716) for which the tumor regions were manually annotated. Of this data, 80% was used for segmentation network training and the remaining 20% was reserved for the internal testing of the segmentation network. With this data, the segmentation network was trained using Adam optimizer for 100 epochs with the dice loss function and an initial learning rate of 10^-3. The learning rate was reduced by a factor of two if the dice loss on the internal validation set (20% of the segmentation training set) did not decrease for 10 consecutive epochs. The model with the best loss on the internal segmentation validation set was selected as a final segmentation model.

Stage two of the DLS, the classification network, was designed using 5 modified DenseNet blocks and it classified tumors into 18 classes using the 3D MRI scans and the segmentation network’s output. The classification network accepted the 3D MRI scans of size 24x256x256 and produced the class probability of each of the tumor classes as an output. In cases where the number of axial slices in the MRI data was less than 24, the input scans were zero-padded to 24 slices. Whereas, for patients with more than 24 slices, data of 24 slices that included the tumor region at the center were analyzed. The classification network was trained using the entire training data with Adam optimizer for 100 epochs the cross-entropy loss function and an initial learning rate of 10^-3. Similar to the segmentation network training, the learning rate was reduced by a factor of two if the loss on the internal validation set (20% of the complete training set) did not decrease for 10 consecutive epochs.
The model with the best loss on the internal validation set was selected as a final classification model.

Moreover, in our dataset, as is the case with the real-world clinical data, all MRI series were not always available for all the patients. Therefore, to accommodate this real-world scenario, using available series from all the patients, we trained a total of 6 architecturally identical models that accepted either a single MRI sequence (T1WI, T2WI, T1C) or a combination of 2 MRI sequences stacked as an input (T1WI & T2WI, T1WI & T1C, T2WI & T2C). At the time of testing, for patients with only one available series, the tumor class predicted by the corresponding series model was considered as a final prediction. For patients with two available series, the majority class predicted by the corresponding 3 models (2 single series models and one combined series model) was considered as a final prediction. For three series scenario, a majority voting was performed on the predictions of all 3 combined series models to determine the final predicted class.

Reference:

1. Ronneberger O, Fischer P, Brox T. U-Net: Convolutional Networks for Biomedical Image Segmentation. Lecture Notes in Computer Science Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015. 2015:234-241. doi:10.1007/978-3-319-24574-4_28.

2. Huang G, Liu Z, Maaten LVD, Weinberger KQ. Densely Connected Convolutional Networks. 2017 IEEE Conference on Computer Vision and Pattern Recognition (CVPR). 2017. doi:10.1109/cvpr.2017.243.
**eFigure 1. Classification of Brain Tumors Included in Study**

(A): List of all the 18 tumor types considered in this study and the distribution of these tumor types in the training dataset.

(B): Representative MRI scans of some of the included tumor types and variations between them.

(Abbreviations: DNET: Dysembryoplastic neuroepithelial tumor)
eFigure 2. Structure of Deep Learning System Used for Brain Tumor Detection and Diagnosis

The structure of the DLS system including the segmentation and classification network. Each encoder block contains one or more convolution steps followed by max-pooling and down-sampling processes. Each time the feature maps are down-sampled, the number of output channels are increased. Each decoder block comprises of one deconvolution (transpose convolution) operation which up-samples the size of the feature maps and correspondingly reduces the number of output channels.
**eFigure 3. Performance of Deep Learning System**

(A) Receiver operating characteristic (ROC) curves of the deep learning system on the test datasets from Tiantan Hospital with 18 classes  
(B) Confusion matrix of DLS with Top-1 prediction, Top-2 prediction, and Top-2-Top-1 predictions.  
(C) The classification accuracy achieved by the neuroradiologists and DLS on the internal test dataset used in the DLS assistance analysis.  
(D) Example showing when neuroradiologists and DLS disagreed, the DLS helped neuroradiologists correct their prediction in 14% of all the test cases.
eFigure 4. Neuroradiologist Diagnosis Performance With or Without Deep Learning System Assistance by Tumor Type

(A-R) ROC diagram and enlarged ROC diagram for acoustic neuroma, pituitary tumor, epidermoid cyst, meningioma, paraganglioma, craniopharyngioma, glioma, hemangioblastoma, metastatic tumor, germ cell tumor, medulloblastoma, DNET, chordoma, lymphomas, choroid plexus papilloma, others, gangliocytoma, hemangiopericytoma respectively. The results were calculated from the 1166 patients independent test dataset and confirmed by the patients’ pathology results. The blue dots denote the performance of the neuroradiologists without DLS assistance; the yellow dots denote the performance of the neuroradiologists with DLS assistance.

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| Manufacturer            | Model         | Thickness (mm) | Resolution (mm*XX/pixel) |
|-------------------------|---------------|----------------|--------------------------|
| GE Medical Systems      | Discovery MR 750 | 6.0,6.3,6.5    | 0.5*0.5                  |
| GE Medical Systems      | Genesis Signa | 6.0,6.5,7.0    | 0.5*0.5                  |
| GE Medical Systems      | Signa HDx     | 6.0,6.5,7.0    | 0.5*0.5                  |
| Philips Healthcare      | Ingenia       | 7.0            | 0.6*0.6/0.4*0.4          |
| Philips Medical Systems | Achieva       | 7.0 or 7.5     | 0.4*0.4/0.3*0.3          |
| Siemens                 | Avanto        | 7.5 -9.8       | 0.4*0.4/0.3*0.3          |
| Siemens                 | TrioTim       | 3.3/6.0-9.1/   | 0.3*0.3/0.5*0.5/0.4*0.4/0.6*0.6/0.7*0.7 |
| Siemens                 | Verio         | 6.0-7.2        | 0.4*0.4/0.3*0.3          |

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| Tumors                  | Classifier                      | Position                      |
|------------------------|--------------------------------|-------------------------------|
|                        | **T1WI** | **T2WI** | **T1C** |                                    |
| Acoustic schwannoma    | ↓        | ↑ /mix   | heterogeneous enhancement | Cerebellopontine Angle |
| Pituitary tumor        | ↓        | ↑        | Homogeneous/weak enhancement | Hypophyseal fossa      |
| Epidermoid cyst        | ↓        | ↑        | None                                          | Multiple extracerebral positions |
| Meningioma             | ↔        | ↔        | moderate homogeneous enhancement, Dural tail sign | Multiple extracerebral positions |
| Paraganglioma          | ↓        | ↑        | Salt and pepper sign                        | Carotid body/ jugular foramen |
| Craniopharyngioma      | ↓ /↔/ ↑  | ↑ /↔/ ↓  | Ring enhancement/calcification               | Suprasellar             |
| Glioma                 | ↓        | ↑        | None/ weak~obvious enhancement               | Brain cortex/subcortical regions |
| Hemangioblastoma       | ↓        | ↑        | Mixed cystic and solid lesion/ Obvious nodular enhancement | Infratentorial          |
| Metastatic tumor       | ↓        | ↑        | Nodular, ring, or punctate enhancement       | Brain cortex/subcortical regions |
| Germ cell tumor        | ↓        | ↑        | Obvious enhancement                          | Basal ganglia/sella area/pineal region |
| Medulloblastoma        | ↔/ ↓     | ↔/ ↑    | Obvious homogeneous enhancement              | Posterior cranial fossa |
| DNET                   | ↓        | ↑        | None/weak enhancement                        | Cerebrum cortex/subcortical regions |
| Chordoma               | mixed ↓  | mixed ↔/ ↓ | Heterogeneous weak enhancement               | Basilar clivus/midline  |
| Lymphomas              | ↔/ ↓     | ↔/ ↓    | Homogeneous obvious enhancement              | Close to the midline    |
| Choroid plexus papilloma | ↔     | ↔       | Homogeneous obvious enhancement/ Mulberry shape | Intracerebroventricular |
| others                 | N.A      | N.A     | N.A.                                          | N.A.                   |
| Gangliocytoma          | ↓        | ↑        | None/ weak enhancement                        | Brain cortex/subcortical regions |

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| Hemangiopericytoma | ↓ | ↑ | Obvious enhancement | extracerebral |
### eTable 3. Age Distribution of Patients in Training Data Sets

| Age    | %     |
|--------|-------|
| 0-1    | 6.7%  |
| 1-10   | 11.7% |
| 10-20  | 11.8% |
| 20-30  | 12.3% |
| 30-40  | 19.0% |
| 40-50  | 17.6% |
| 50-60  | 15.4% |
| 60-70  | 4.4%  |
| 70-80  | 1.0%  |
| 80-90  | 0.1%  |

### eTable 4. Age Distribution of Patients in All Test Data Sets

| Age    | Tiantan Hospital (%) | Shanxi Hospital (%) | Jilin Hospital (%) | 301 Hospital (%) |
|--------|----------------------|---------------------|--------------------|------------------|
| 1-10   | 10.9                 | -                   | 1.4                | 1.4              |
| 10-20  | 14.6                 | -                   | 8.6                | 5.1              |
| 20-30  | 10.5                 | 2.0                 | 2.9                | 9.3              |
| 30-40  | 19.9                 | 10.9                | 10.0               | 15.8             |
| 40-50  | 21.7                 | 25.7                | 14.3               | 26.5             |
| 50-60  | 15.0                 | 24.8                | 31.4               | 24.3             |
| 60-70  | 6.7                  | 31.7                | 27.1               | 15.0             |
| 70-80  | 0.7                  | 5.0                 | 1.4                | 2.5              |
| 80-90  | -                    | -                   | 2.9                | -                |
**eTable 5. Tumor Type Statistics in Training Data Sets**

| Index | Tumor type                                      | Number of cases for training | Number of cases for segmentation training | Number of cases for classifier training | Number of cases in validation set | Number of pathologies |
|-------|-----------------------------------------------|------------------------------|-------------------------------------------|----------------------------------------|----------------------------------|-----------------------|
| 1     | Epidermoid cyst                              | 1157                         | 885                                       | 930                                    | 227                             | 525                   |
| 2     | Pituitary adenoma                            | 4433                         | 1163                                      | 3329                                   | 1104                            | 525                   |
| 3     | Paraganglioma (Glomus jugulare tumor)        | 51                           | 48                                        | 38                                     | 13                              | 11                    |
| 4     | Chordoma                                      | 792                          | 586                                       | 649                                    | 143                             | 335                   |
| 5     | Gangliocytoma / ganglioglioma                 | 509                          | 304                                       | 423                                    | 86                              | 291                   |
| 6     | Lymphoma                                      | 693                          | 377                                       | 530                                    | 163                             | 94                    |
| 7     | Craniopharyngioma                            | 2628                         | 675                                       | 1910                                   | 718                             | 735                   |
| 8     | Choroid plexus papilloma                     | 317                          | 206                                       | 207                                    | 110                             | 115                   |
| 9     | Meningioma                                    | 5840                         | 514                                       | 4168                                   | 1672                            | 966                   |
| 10    | Medulloblastoma                               | 716                          | 468                                       | 500                                    | 216                             | 317                   |
| 11    | Germ cell tumors (including Germinoma and Teratoma) | 910 | 489 | 583 | 327 | 273 |
| 12    | Acoustic neuroma                              | 3366                         | 891                                       | 2404                                   | 962                             | 1136                  |
| 13    | Hemangioblastoma                              | 730                          | 433                                       | 617                                    | 113                             | 305                   |
| 14    | Hemangiopericytoma                            | 293                          | 194                                       | 225                                    | 68                              | 176                   |
| 15    | Dysembryoplastic neuroepithelial (DNET)       | 257                          | 110                                       | 183                                    | 74                              | 153                   |
| 16    | Metastasis                                    | 727                          | 68                                        | 609                                    | 118                             | 122                   |
| 17    | Glioma                                        | 10659                        | 3927                                      | 8631                                   | 2028                            | 3758                  |
| 18    | Other brain tumors (Including Dermoid cysts, Granular cell tumors, Melanocytic tumors) | 3793 | 378 | 2467 | 1326 | 146 |
|       | Total                                         | 37871                        | 11716                                     | 28403                                  | 9468                            | 9983                  |

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**eTable 6.** Brain Tumor Distribution in All Data Sets

|                    | Training & validation Set | Test Set 1 | Test set 2 |
|--------------------|---------------------------|------------|------------|
|                    | Tiantan Hospital | Shanxi Hospital | Jilin Hospital | 301 Hospital | Tiantan Hospital |
| 1 Epidermoid cyst  | 1157            | 19          | 2           | 2           | 0            | 74           |
| 2 Pituitary adenoma| 4433            | 17          | 27          | 5           | 185          | 64           |
| 3 Paraganglioma    | 51              | 10          | 0           | 1           | 27           | 22           |
|                    | (Glomus jugulare tumor) |          |             |             |              |              |
| 4 Chordoma         | 792             | 17          | 2           | 1           | 2            | 68           |
| 5 Gangliocytoma / | 509             | 12          | 1           | 1           | 0            | 46           |
| ganglioglioma      |                |             |             |             |              |              |
| 6 Lymphoma         | 693             | 13          | 4           | 3           | 23           | 42           |
| 7 Craniopharyngioma| 2628            | 18          | 2           | 5           | 22           | 74           |
| 8 Choroid plexus   | 317             | 10          | 0           | 1           | 8            | 42           |
| papilloma          |                |             |             |             |              |              |
| 9 Meningioma       | 5840            | 18          | 32          | 25          | 205          | 76           |
| 10 Medulloblastoma | 716             | 11          | 3           | 1           | 11           | 33           |
| 11 Germ cell tumors| 910             | 14          | 1           | 1           | 8            | 56           |
| 12 Acoustic neuroma| 3366            | 19          | 25          | 2           | 160          | 61           |
| 13 Hemangioblastoma| 730             | 13          | 0           | 1           | 11           | 44           |
| 14 Hemangiopericytoma| 293          | 9           | 0           | 0           | 2            | 31           |
| 15 Dysembryoplastic neuroepithelial | 257   | 13          | 0           | 0           | 1            | 49           |
|                    |                |             |             |             |              |              |
| 16 Metastasis      | 727             | 9           | 0           | 4           | 31           | 42           |
| 17 Glioma and its subtypes | 10659 | 69          | 0           | 18          | 169          | 294          |
| 18 Other brain tumors | 3793         | 9           | 0           | 0           | 4            | 48           |
| **Total**          | 37871          | 300         | 99          | 71          | 869          | 1166         |

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### eTable 7. Magnetic Resonance Imaging Manufacturer Distribution in All Test Data Sets

| Test center   | Manufacturer          | Model               | %   |
|---------------|-----------------------|---------------------|-----|
| Tiantan Hospital | GE Medical Systems | Signa HDe          | 21.1|
|               | GE Medical Systems    | Genesis Signa       | 18.8|
|               | GE Medical Systems    | Discovery MR 750    | 8.7 |
|               | Siemens               | TrioTim             | 33.9|
|               | Siemens               | Verio               | 15.8|
|               | Toshiba               | MRT200F3            | 1.3 |
|               | Unknown               | Unknown             | 0.3 |
| Shanxi Hospital  | Siemens             | TrioTim             | 75.7|
|                | Siemens               | Avanto              | 17.4|
|                | GE Medical Systems    | Discovery MR 750    | 7.0 |
| Jilin Hospital   | GE Medical Systems   | Ingenia             | 6.3 |
|                | Siemens               | Avanto              | 39.2|
|                | Siemens               | TrioTim             | 7.6 |
|                | Philips Medical systems | Achieva            | 27.8|
|                | Philips Medical systems | Ingenia            | 15.2|
|                | Neusoft               | NSM-S15P            | 2.5 |
|                | UIH                   | uMR 780             | 1.3 |
| 301 Hospital     | GE Medical Systems   | Signa HDxt          | 56.5|
|                | GE Medical Systems    | DISCOVERY MR750     | 22.6|
|                | GE Medical Systems    | SIGNA EXCITE        | 4.8 |
|                | GE Medical Systems    | SIGNA HDxt          | 4.8 |
|                | GE Medical Systems    | Optima MR360        | 1.3 |
|                | Siemens               | Skyra               | 0.7 |
|                | Siemens               | Espree              | 0.2 |
|                | UIH                   | uMR 770             | 8.4 |
|                | alltech               | EchoStar            | 0.1 |
|                | Centauri              | Centauri            | 0.3 |