Adult Glioma: Grading and Treatment

Glioma Grading and Classification

While most cancers are staged, adult gliomas are “graded.” There are 4 grades of brain tumors: I, II, III, and IV. I and II are called low grade. Grades III and IV are high grade. The grade of a tumor is determined by how much and how fast it may grow.

- **Grade I** are slow growing and the cells almost look normal under a microscope.
- **Grade II** are fairly slow growing, look a little bit abnormal, can spread to normal tissue, and can recur (come back) as a higher-grade tumor.
- **Grade III** are actively making more abnormal cells, look abnormal under a microscope, spread to nearby normal tissue, and tend to recur as a higher grade.
- **Grade IV** are abnormal cells that multiply quickly. They look abnormal under a microscope, form new blood vessels to keep growing, and there are areas of dead (necrotic) tissue in the middle of the tumor.

Gliomas are also classified. The grade and classification help figure out the best plan of care. The World Health Organization (WHO) classifies adult gliomas by looking at:

- **The type of cell the tumor starts in (tumor type):** Gliomas are tumors that start in glial cells. There are many types of glial cells. The different types of gliomas are based on the type of glial cell they started in:
  - **Astrocytoma (including glioblastomas):** These are tumors that start in glial cells called astrocytes. These tumors are often hard to remove with surgery. They may spread into the cerebrospinal fluid (CSF), but they don’t often spread outside of the brain or spinal cord. They can be low or high grade.
  - **Oligodendrogliomas:** These tumors start in glial cells called oligodendrocytes. These tend to grow slowly. Most of these tumors can spread into nearby brain tissue, making it hard to remove the whole tumor with surgery. Oligodendrogliomas can spread into the CSF, but they don’t often spread outside the brain or spinal cord. These are grade II tumors.
  - **Ependymomas:** These tumors start in ependymal cells and often grow in the ventricles (pathways in your brain) or spinal cord. Ependymomas are more likely to spread into CSF, but don’t often spread outside the brain or spinal cord. These tumors can block the flow of CSF into the ventricles, causing your ventricles to swell and enlarge, called hydrocephalus. They are often grade II or III tumors.
- **The grade of the tumor:** Some types of brain and spinal cord tumors are more likely to grow into nearby brain or spinal cord tissue and grow more quickly. These types of tumors are split into 4 grades, based on how the cancer cells look under a microscope:
  - **Lower grade (grade I or II) tumors:** Often grow slowly and are less likely to grow into nearby tissues.
  - **Higher grade (grade III or IV):** Often grow quickly and are more likely to grow into nearby tissues.
- **Gene changes (mutations):** There may be changes to genes found in your tumor cells. Many types of brain and spinal cord tumors are now tested for mutations in one of the IDH genes (IDH1 or IDH2). Other gene mutations can also be linked to some types of tumors. Talk with your provider about whether you will be tested for gene mutations.
- **Where the tumor is:** This can affect the symptoms it may cause, as well as which treatments work best.
for you.

You may also have tests like blood work, PET scan, lumbar puncture (LP), CT scan/CT angiography (CTA), and MRI. You may also have a biopsy. Surgery to do a biopsy is needed to find out the grade and type of your glioma. Two types of biopsies used are:

- **Stereotactic (needle) biopsy:** A small piece of the tumor is taken out because the whole tumor can’t be removed. This piece of tumor is then sent to a lab to be looked at under a microscope.
- **Surgical or open biopsy (craniotomy):** This is surgery that removes a part of your skull to get to the tumor. Craniotomy is used if your surgeon thinks all or most of the tumor can be removed with surgery. If most of the tumor, but not all, can be removed, it is called “debulking” the tumor. The tumor that is removed is looked at under a microscope while you are still in the operating room (OR) so that more surgery may be done at the same time if needed.

These tests are done to learn about your cancer and your health so that a plan of care can be made for you.

### How is adult glioma graded?

- **Low-grade (grade I or II) Astrocytomas:**
  - **Non-infiltrating (grade I) astrocytomas** do not often grow into nearby tissues. Examples are pilocytic astrocytomas and subependymal giant cell astrocytomas (SEGAs).
  - **Grade II astrocytomas** tend to grow more slowly, but they can grow into nearby areas, making them harder to remove with surgery. These tumors can become more aggressive and faster growing over time. Examples are diffuse astrocytomas and pleomorphic xanthoastrocytomas (PXAs).

- **High-grade (grade III or IV) Astrocytomas:**
  - **Anaplastic (grade III) astrocytomas** tend to grow quickly and spread into nearby brain tissue.
  - **Glioblastomas (grade IV)** are the fastest growing type of glioma. These tumors make up more than half of all gliomas and are the most common cancerous brain tumors in adults.

- **Low-grade (grade II) Oligodendrogliomas**
  - **Grade II oligodendrogliomas** are low grade tumors. These tumors grow slowly and spread into nearby normal tissue. These tumors do not cause symptoms at first.

- **High-grade (grade III) Oligodendrogliomas**
  - **Grade III oligodendrogliomas** are fast-growing tumors. They are called anaplastic oligodendrogiomas.

- **Low-grade (grade I or II) Ependymomas**
  - **Grade I ependymomas** grow slowly. These tumors include subependymoma and myxopapillary ependymoma. Myxopapillary tumors often occur in the spine.
  - **Grade II ependymomas** can occur in the brain or the spine.

- **High-grade (grade III) Ependymomas**
  - **Grade III ependymomas** are fast-growing tumors. This type of tumor is also called “anaplastic ependymomas.” These most often occur in the brain but can also occur in the spine.

### How is adult glioma treated?

Treatment for adult glioma depends on many things, like what type of tumor you have, where the tumor is, your age, overall health, and testing results. More than one type of treatment is often used for adult gliomas. Your treatment may include some or all the following:

- Surgery.
- Radiation therapy.
Surgery
Surgery is the main treatment for gliomas because surgery is needed to grade and classify your tumor. Surgery is often used with other treatment options, like chemotherapy and/or radiation therapy (see below). Surgery to diagnose and treat a brain tumor is called a craniotomy.

The goals of surgery are to:

- Grade the glioma.
- Improve symptoms by making the tumor smaller in size.
- Remove all of the tumor if possible. If not, remove as much of the tumor as possible (debulking).

Most symptoms of gliomas are caused by too much pressure in the brain or compression (pushing down) of brain tissue. By removing some (if not all) of the tumor, there is less pressure and compression in the brain, improving symptoms.

Radiation Therapy
Radiation therapy uses high-energy x-rays to kill cancer cells. Radiation may be used:

- After you have had surgery to take out as much of the tumor as possible. This is done to try to kill any cancer cells that were left.
- To help lessen or prevent symptoms caused by the tumor.
- If you are not able to have surgery to take out some or all of the tumor.

There are a few types of radiation that may be used to treat adult glioma:

- **External beam radiation therapy (EBRT)** - The source of radiation comes from outside of the body and focuses on the tumor. There are a few kinds of EBRT that may be used, depending on the type of tumor:
  - Three-dimensional conformal radiation therapy (3D-CRT).
  - Intensity modulated radiation therapy (IMRT).
  - Volumetric modulated arc therapy (VMAT).
  - Conformal proton beam radiation therapy.
  - Stereotactic radiosurgery (SRS)/stereotactic radiotherapy (SRT).
  - Image-guided radiation therapy (IGRT).
  - Whole brain and spinal cord radiation therapy (craniospinal radiation).

- **Brachytherapy** - The source of radiation comes from inside your body. Radioactive material is placed directly into or near the tumor. Brachytherapy is often used along with EBRT.

Chemotherapy
Chemotherapy is the use of medications to kill cancer cells. Chemotherapy can be a pill that you take by mouth or a liquid that is given through an IV into your bloodstream (intravenous). For chemotherapy to be able to kill glioma cells, it must be able to pass from the bloodstream into the brain. The brain is protected by the blood-brain-barrier. The blood-brain-barrier prevents many toxins and chemicals (including some medicines) from entering and hurting the brain. For this reason, chemotherapy used to treat glioma has to be able to cross this barrier so it can reach the tumor. These medications can be given alone or with other chemotherapies.

Some of the chemotherapies used to treat brain and spinal cord tumors are:

- Carboplatin.
- Carmustine (BCNU) - Comes in IV form as well as in a gel wafer that can be placed during surgery. The
wafer is placed on any tumor that cannot be removed with surgery and dissolves directly into the tumor.

- Cisplatin.
- Cyclophosphamide.
- Etoposide.
- Irinotecan.
- Lomustine (CCNU).
- Methotrexate.
- Procarbazine.
- Temozolomide.
- Vincristine.

**Targeted Therapy**

Targeted therapies use medications to target genes and proteins that control how cancer cells grow, divide, and spread. This slows down or kills the cancer cells while keeping the normal cells as safe as possible. Research is ongoing with the use of targeted therapy for gliomas. Two targeted therapies that are being used are bevacizumab and everolimus.

**Treatment with other Medications**

Steroids, like prednisone or dexamethasone, may be a part of your glioma treatment. Steroids are anti-inflammatory medications that are used to decrease swelling in the brain from the tumor itself or treatment. Some common side effects of steroids are infection, stomach ulcers or bleeding, weight gain, having a hard time sleeping, and mood changes.

If your tumor is causing you to have seizures, you may be started on anti-seizure medications (called anticonvulsants).

If your tumor is near your pituitary gland, your hormone levels may be affected. Based on blood work and symptoms, your care team may start you on hormone therapy.

**Clinical Trials**

You may be offered a clinical trial as part of your treatment plan. To find out more about current clinical trials, visit the [OncoLink Clinical Trials Matching Services](http://www.oncolink.org).

**Making Treatment Decisions**

Your care team will make sure you are included in choosing your treatment plan. This can be overwhelming as you may be given a few options to choose from. It feels like an emergency, but you can take a few weeks to meet with different providers and think about your options and what is best for you. This is a personal decision. Friends and family can help you talk through the options and the pros and cons of each, but they cannot make the decision for you. You need to be comfortable with your decision – this will help you move on to the next steps. If you ever have any questions or concerns, be sure to call your team.

You can learn more about [brain and spinal cord cancers](http://www.oncolink.org) at OncoLink.org.

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