

Glioblastoma

Alternative Treatment Report

How to Enhance Radiation Treatment

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You should consult with your doctor before making any changes in your cancer treatment program. It may be helpful to give this report to your doctors when requesting a change in your cancer treatment program.

I've left some of the scientific and medical terms in this report for your doctors. I'm sorry that they are difficult to understand. In some cases I've included a link to www.naturalcancerreports.com/Cancer-Terminology.html for an explanation of many of these words.

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Enhancing Glioblastoma Radiation Treatment*

How to enhance Glioblastoma multiforme radiation treatment with medications, dietary supplements and lifestyle changes.*

Research based information showing how targeted medications, dietary supplements and lifestyle changes may enhance your Glioblastoma multiforme treatment.

Malignant gliomas are the most common primary brain tumor, accounting for more than half of the more than 18,000 primary malignant brain tumors diagnosed each year in the United States. These tumors are the second-most common cause of cancer death in the 15 to 44 age group.¹

Surgery is recommended for all operable brain tumors and is usually followed by radiation therapy. Several studies have shown that adding chemotherapy to radiation treatment can improve patients' survival. In June 2004 researchers announced that adding the drug temozolomide (Temodar®) to radiation therapy increased median survival in patients with glioblastoma multiforme (GBM) by about two months. This approach is now considered the standard of care for the initial treatment of these tumors.²

Malignant gliomas are a class of brain tumors that are resistant to radiation and chemotherapeutic drugs, contributing to the poor prognosis associated with these tumors.

There are few human studies due to the aggressiveness of glioblastoma multiforme tumor growth and moral/ethical issues. Therefore most glioblastoma research is based on animal and laboratory cell studies.

The following research is specific for Glioblastoma multiforme and Radiation Treatment. There are few research studies since this cancer is less common than most other cancers. It's possible some of the following natural products, even though not researched or studied, may enhance the effectiveness of radiation treatment for Glioblastoma. Additional research information is available in our Natural Cancer Report on Radiation Therapy.

A positive cell culture study typically leads to animal studies. Positive animal studies typically lead to human studies. A positive or encouraging dietary supplement or medication cell culture study does not always provide the same results in animal or human studies.

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Medications

Dexamethasone / Celecoxib

Restricting glucocorticoid (steroid, cortisone, dexamethasone) in the treatment of patients with a solid tumor may help improve outcomes. Celecoxib (Celebrex®) rather than dexamethasone to prevent brain edema was given to a patient with Glioblastoma upon the patient's request. The patient did not require dexamethasone for the entire treatment. Dexamethasone administration hence was avoided successfully in this case.³

In a Glioblastoma multiforme laboratory cell culture dexamethasone decreased the effectiveness of Temozolomide (Temodar).⁴

A requirement of dexamethasone dose greater than 4 mg at the end of Radiation Therapy was associated with worse survival.⁵

Germany doctors state "*Effort should be taken to minimize corticosteroid doses, since both steroids and temozolomide lead to immunosuppression.*"⁶

Dexamethasone does decrease swelling in the brain. But at the same time it elevates blood glucose levels which feed GBM cells.

Consult your physician before decreasing or discontinuing your steroid, cortisone or dexamethasone treatment. Sudden discontinuation of this medication can have very serious side effects and possible death. Your doctor can tell you how to slowly decrease and stop the medication if indicated.

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Medications

Celecoxib (Celebrex®)

Celecoxib significantly enhanced glioblastoma radiosensitivity, reduced cancer cell survival, and prolonged survival of glioblastoma-implanted mice by inhibition of tumor angiogenesis with extensive tumor necrosis.⁷

Some Glioblastoma multiforme cells express inflammatory COX-2 and tend to be resistant to radiation treatment. Blocking COX-2 may lower the required dose of postoperative radiation. Increasing the COX-2 inhibitor concentration yielded higher cell kill. COX-2 inhibitors may have a role radiosensitizing otherwise radioresistant forms of glioblastoma multiforme.⁸ Celecoxib (Celebrex®) is a COX-2 inhibitor.

Many dietary supplements have COX-2 inhibitor properties including curcumin in [CurcuPlex Cr.](#)

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Medications

Temozolomide (Temodar®)

Combining Temozolomide and radiation treatment prolongs length of survival.⁹

Temozolomide provides additive tumor cell damage in combination with radiation. Combining Temozolomide and radiation yielded additive cytotoxicity, but only when Temozolomide was delivered 72 hours before radiation. According to researchers Temozolomide treatment should commence at least 3 days before radiation to achieve maximum benefit.¹⁰

[Click here to get your Report: How to Enhance Temozolomide Temodar Glioblastoma Treatment.](#)

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Dietary Supplements

Copper

Studies in humans and animals show that high blood levels of copper are associated with tumor incidence, tumor burden, malignant progression, and recurrence in Hodgkin's lymphoma, sarcoma, leukemia, and cancers of the cervix, **brain**, breast, liver, and lung.

Copper metabolism is upregulated, and the extra copper is transported to tumor tissue.

When copper levels are reduced, the tumors stop building new blood vessels to bring in nutrients and oxygen. Without copper, the tumors eventually stop growing, and in some cases, even shrink.^{11 12}

One published study demonstrated that lowering copper levels with penicillamine (injection chelation) did not improve survival in patients undergoing radiation for glioblastoma multiforme.¹³

Copper is a mineral necessary for many body functions. But, many of us get too much copper from the copper water pipes and brass faucets in our home and at work.

If you have copper pipes at home or work **do not** take a multiple vitamin with copper.

You can test for copper toxicity at <http://www.toxicwatersolution.com/Heavy-Metal-Test/Heavy-Metal-Testing/>

If you are toxic you can take a supplement to lower copper levels.

<http://www.toxicwatersolution.com/Dietary-Supplements-Oral-Chelation.html>

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Curcumin/turmeric

Curcumin was tested on human and rat glioma cancer cell lines in a laboratory study.

Curcumin sensitized glioma cells to radiation. Researchers state, *“These findings support the role for curcumin as an adjunct to traditional radiation in the treatment of brain cancer.”*¹⁴

At the time of publication this is the only curcumin Glioblastoma radiation study.

Curcumin and curcumin extracts are not well absorbed and are barely measurable in the blood after oral dosage. Researchers and manufacturers have found that piperine, an enhancer of curcumin bioavailability in humans, potentiates the apoptotic effect of curcumin against medulloblastoma cells. Curcumin and piperine combination downregulated Bcl-2, suppressed cell proliferation and triggered cell-cycle arrest at G(2) phase. Curcumin and piperine enhances the killing efficiency of nontoxic doses of cisplatin and gamma-rays. Researcher state, *“These results indicate that curcumin, a natural nontoxic compound, represents great promise as Shh-targeted therapy for medulloblastomas.”*¹⁵

[Click here to learn about CurcuPlex CR.](#)

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EPA (eicosapentaenoic acid) (omega-3)

EPA was added to HT-29 and U251 glioblastoma cells grown in a research laboratory. When the cancer cells were irradiated researchers found EPA enhanced the effectiveness of radiation on both cell lines.¹⁶

[Click her to learn more about OmegaPure 780.](#)

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Green tea extract/EGCG

Epigallocatechin gallate (EGCG) is the most abundant catechin in tea. It is an antioxidant that has therapeutic properties for many disorders including glioblastoma brain cancer.^{17 18 19} High amounts are found in green tea but not black tea. Concentrated EGCG can be found in many supplements.

U-87 human Glioblastoma multiforme (GBM) cells, grown in a laboratory, pretreated with EGCG extract exhibited a dose-dependent decrease in their proliferation rate with radiation treatment. Radiation resistant glioblastoma multiforme cells (containing Survivin) pretreated with EGCG became sensitive to radiation treatment and their RhoA expression was down regulated. Researchers state *“the combination of natural anti-cancerous molecules such as EGCG with radiotherapy could improve the efficacy of ionizing radiation treatments.”*²⁰

Most studies of other cancers show that it takes close to 9 cups of green tea to get an anti-cancer effect. That is a lot of green tea! A quality green tea extract capsule can be equal to 10 cups of green tea with typically a fraction of the caffeine. Click here for information on [Green Tea 600™](#). Usual dose is 1 capsule 3 times daily at breakfast, lunch and midafternoon if the caffeine is tolerated.

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Resveratrol

Laboratory treatment of glioblastoma multiforme cells CD133(+) with resveratrol induced apoptosis and enhanced radiosensitivity by suppressing STAT3 signaling. Resveratrol facilitated the differentiation of CD133(+) into CD133(-) or astrocytoma cells. Researchers then transplanted glioblastoma multiforme cells into animals. Resveratrol treatment significantly improved the animal's survival rate and synergistically enhanced the radiosensitivity of radiation.²¹

Resveratrol is a polyphenol found in several plant species. U87 glioma cells were grown in a laboratory and treated with resveratrol and/or X rays. Resveratrol induces a delay in cell cycle progression (cancerous type cell growth) and both alone and in combination with X rays is able to enhance gap junction Intercellular Communications.²²

Click here for information about [Resveratin plus™](#).

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Diet and Lifestyle

Diet

A ketogenic diet can target energy metabolism in brain tumors. Following incomplete surgical resection a 65 year old female followed a Ketogenic diet and took vitamins and minerals with the traditional glioblastoma multiforme treatment. She followed a restrictive 4:1 (fat:carbohydrate + protein) **ketogenic diet** that delivered 600 calories per day. Steroid medication (dexamethasone) was removed during the course of treatment.

After two months of treatment, the patient's body weight was reduced by about 20% and no brain tumor tissue was detected with PET or MRI imaging. Blood glucose was reduced and urinary ketones were elevated.

MRI evidence of tumor recurrence was found 10 weeks after suspension of strict diet therapy.²³

Ketone urine strips are available at your pharmacy. Use the **Ketogenic Food List** to help keep you in the "Fat Burning Zone".

Glucose

Tumor cells rely preferentially on low oxygen glucose energy production rather than on high oxygen respiration for ATP energy generation, a phenomenon known as the Warburg effect. Researchers found that glucose withdrawal induces extensive **apoptosis** in glioblastoma multiforme cells. ATP energy levels are sustained on glucose withdrawal due to elevation of fatty acid oxidation and ensuing respiration. Fatty acid generated oxidative stress generated in the mitochondrial respiratory chain is the direct cause of cell

death in glioblastoma multiforme cells. The fatty acid oxidative stress only occurs in glioblastoma multiforme cells. Glucose withdrawal induced normal cell death in the malignant glioblastoma cells. Glycolysis (energy production from glucose) was a potentially efficient and selective target for glioblastoma multiforme treatment.²⁴

Glycemic Index Foods of less than 70 should be consumed.

Typically 3 small meals and 3 small snacks should be consumed each day to control blood glucose levels. Additional prescription and natural products can help keep blood glucose levels in ideal ranges.

Purchase or borrow a friend's glucose meter and check your blood glucose (sugar) after not eating for 12 hours and 2 hours after eating a large meal.

Fasting Glucose: Ideal 80-90, (> 100 is pre diabetes level, > 110 is diabetes level)
2 hours After a Meal Ideal: <125 (> 140 is diabetes level).

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Oxygen (hypoxia)

Increasing malignancy of gliomas correlates with an increase in cellularity and a poorly organized tumor vasculature leading to insufficient blood supply, hypoxic areas and ultimately to the formation of necrosis, a characteristic of glioblastoma.

Hypoxic/necrotic tumors are more resistant to chemotherapy and radiation. Hypoxia induces either directly or indirectly (through the activation of transcription factors) changes in the biology of a tumor and its microenvironment leading to increased aggressiveness and tumor resistance to chemotherapy and radiation.²⁵

An understanding of the role of hypoxia in tumor development and growth is important for physicians involved in the care of patients with brain tumors.²⁶

Any exercise that increases the heart rate and makes it hard to talk or breath will increase your oxygen levels throughout the body including the brain. Exercising once daily is not sufficient. Moderate activity/exercise should be done every couple of hours a few moments at a time.

A Pulse Oximeter (pulse ox) can be used to monitor your oxygen saturation level before, during and after exercise. I recommend that my clients have a number greater than 97. It is usually placed on a finger and may have a red light. Pulse Oximeters are available on the internet for less than \$50.

Oxygen is available via prescription from your doctor. Few doctors will prescribe oxygen treatment for cancer unless your oxygen level (pulse ox) is low.

If you live in large metropolitan areas you can check the internet and telephone book for oxygen bars. Used oxygen concentrators, tubing, masks and nasal cannulas are available on the internet or craigslist.org and in some cases can be shipped directly to your home.

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In my practice I use

- [CurcuPlex CR](#)
- [Green Tea 600](#)
- [OmegaPure 780](#)

Cancer Vitamin Purchase

You may go online to purchase these products directly through the manufacture at:

Xymogen

<http://store.xymogen.com/>

Code #: NCS4ME

Practitioner Last Name: Bishop

Natural Cancer Treatment Appointments

I'm available to integrate and customize your cancer supplement and food program for radiation, chemotherapy and prevention.

Learn more at:

<http://www.naturalcancerreports.com/Alternative-Cancer-Treatment-Appointments.html>

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References

¹ www.Cancer.gov

² Patterns of care for adults with newly diagnosed malignant glioma. Chang SM, Parney IF, Huang W, Anderson FA Jr, Asher AL, Bernstein M, Lillehei KO, Brem H, Berger MS, Laws ER; Glioma Outcomes Project Investigators. *JAMA*. 2005 Feb 2;293(5):557-64.

³ Avoiding glucocorticoid administration in a neurooncological case. Rutz HP, Hofer S, Peghini PE, Gutteck-Amsler U, Rentsch K, Meier-Abt PJ, Meier UR, Bernays RL. *Cancer Biol Ther*. 2005 Nov;4(11):1186-9.

⁴ Dexamethasone protected human glioblastoma U87MG cells from temozolomide induced apoptosis by maintaining Bax:Bcl-2 ratio and preventing proteolytic activities. Das A, Banik NL, Patel SJ, Ray SK. *Mol Cancer*. 2004 Dec 8;3(1):36.

⁵ Improved median survival for glioblastoma multiforme following introduction of adjuvant temozolomide chemotherapy. Back MF, Ang EL, Ng WH, See SJ, Lim CC, Chan SP, Yeo TT. *Ann Acad Med Singapore*. 2007 May;36(5):338-42.

⁶ Efficacy and toxicity of postoperative temozolomide radiochemotherapy in malignant glioma. Kocher M, Kunze S, Eich HT, Semrau R, Müller RP. *Strahlenther Onkol*. 2005 Mar;181(3):157-63.

⁷ Enhancement of glioblastoma radioresponse by a selective COX-2 inhibitor celecoxib: inhibition of tumor angiogenesis with extensive tumor necrosis. Kang KB, Wang TT, Woon CT, Cheah ES, Moore XL, Zhu C, Wong MC. *Int J Radiat Oncol Biol Phys*. 2007 Mar 1;67(3):888-96.

⁸ Differential cyclooxygenase-2 enzyme expression in radiosensitive versus radioresistant glioblastoma multiforme cell lines. Karim A, McCarthy K, Jawahar A, Smith D, Willis B, Nanda A. *Anticancer Res*. 2005 Jan-Feb;25(1B):675-9.

⁹ *Lancet Oncol*. 2009 May;10(5):459-66. Epub 2009 Mar 9. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Stupp R, Hegi ME, Mason WP, et al.

¹⁰ *Int J Radiat Oncol Biol Phys*. 2009 Dec 1;75(5):1511-9. Cytotoxic effects of temozolomide and radiation are additive- and schedule-dependent. Chalmers AJ, Ruff EM, Martindale C, Lovegrove N, Short SC.

¹¹ *J Natl Cancer Inst*. 2000 Aug 2;92(15):1202-3. Cutting copper curbs angiogenesis, studies show. Vanchieri C.

¹² *Klin Wochenschr*. 1984 Feb 15;62(4):187-9. Serum ceruloplasmin and copper levels in patients with primary brain tumors. Turecký L, Kalina P, Uhlíková E, Námerová S, Krizko J.

¹³ *Neuro Oncol*. 2005 Jul;7(3):246-53. Phase 2 trial of copper depletion and penicillamine as antiangiogenesis therapy of glioblastoma. Brem S, Grossman SA, Carson KA, New P, Phuphanich S, Alavi JB, Mikkelsen T, Fisher JD; New Approaches to Brain Tumor Therapy CNS Consortium. Department of Interdisciplinary Oncology and Neurosurgery, University of South Florida College of Medicine and Neuro-Oncology Program, H. Lee Moffitt Cancer Center, Tampa, FL 33620, USA.

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¹⁴ *J Neurochem*. 2007 Jul;102(2):522-38. Curcumin suppresses growth and chemoresistance of human glioblastoma cells via AP-1

and NFkappaB transcription factors. Dhandapani KM, Mahesh VB, Brann DW.

¹⁵ *Mol Carcinog*. 2009 Dec 18. Curcumin inhibits the Sonic Hedgehog signaling pathway and triggers apoptosis in medulloblastoma cells. Elamin MH, Shinwari Z, Hendrayani SF, Al-Hindi H, Al-Shail E, Khafaga Y, Al-Kofide A, Aboussekhra A.

¹⁶ *Strahlenther Onkol*. 2011 Feb;187(2):127-34. Omega-3 fatty acid supplementation in cancer therapy : does eicosapentanoic acid influence the radiosensitivity of tumor cells? Manda K, Kriesen S, Hildebrandt G, Fietkau R, Klautke G. Source Department of Radiotherapy, University of Rostock, Rostock, Germany. katrin.manda@uni-rostock.de

¹⁷ Inhibitory effect of epigallocatechin-gallate on brain tumor cell lines in vitro. Yokoyama S, Hirano H, Wakimaru N, Sarker KP, Kuratsu J. *Neuro Oncol*. 2001 Jan;3(1):22-8.

¹⁸ Epigallocatechin-3 gallate selectively inhibits the PDGF-BB-induced intracellular signaling transduction pathway in vascular smooth muscle cells and inhibits transformation of sis-transfected NIH 3T3 fibroblasts and human glioblastoma cells (A172). Ahn HY, Hadizadeh KR, Seul C, Yun YP, Vetter H, Sachinidis A. *Mol Biol Cell*. 1999 Apr;10(4):1093-104.

¹⁹ Green tea compounds inhibit tyrosine phosphorylation of PDGF beta-receptor and transformation of A172 human glioblastoma. Sachinidis A, Seul C, Seewald S, Ahn H, Ko Y, Vetter H. *FEBS Lett*. 2000 Apr 7;471(1):51-5.

²⁰ The Survivin-mediated radioresistant phenotype of glioblastomas is regulated by RhoA and inhibited by the green tea polyphenol (-)-epigallocatechin-3-gallate. McLaughlin N, Annabi B, Bouzeghrane M, Temme A, Bahary JP, Moundjian R, Béliveau R. *Brain Res*. 2006 Feb 3;1071(1):1-9. Epub 2006 Jan 10.

²¹ *J Cell Physiol*. 2011 Apr 18. doi: 10.1002/jcp.22806. Resveratrol suppresses tumorigenicity and enhances radiosensitivity in primary glioblastoma tumor initiating cells by inhibiting the STAT3 axis. Yang YP, Chang YL, Huang PI, Chiou GY, Tseng LM, Chiou SH, Chen MH, Chen MT, Shih YH, Chang CH, Hsu CC, Ma HI, Wang CT, Tsai LL, Yu CC, Chang CJ. Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan.

²² *Mol Carcinog*. 2008 Aug;47(8):587-98. Resveratrol and X rays affect gap junction intercellular communications in human glioblastoma cells. Leone S, Fiore M, Lauro MG, Pino S, Cornetta T, Cozzi R.

²³ *Nutr Metab (Lond)*. 2010 Apr 22;7:33. Metabolic management of glioblastoma multiforme using standard therapy together with a restricted ketogenic diet: Case Report. Zuccoli G, Marcello N, Pisanello A, Servadei F, Vaccaro S, Mukherjee P, Seyfried TN. Radiology Department, Arcispedale Santa Maria Nuova, Reggio E, 42100, Italy. giulio.zuccoli@gmail.com.

²⁴ Glucose withdrawal induces oxidative stress followed by apoptosis in glioblastoma cells but not in normal human astrocytes. Jelluma N, Yang X, Stokoe D, Evan GI, Dansen TB, Haas-Kogan DA. *Mol Cancer Res*. 2006 May;4(5):319-30.

²⁵ Hypoxia helps glioma to fight therapy. Amberger-Murphy V. *Curr Cancer Drug Targets*. 2009 May;9(3):381-90.

²⁶ Brain tumor hypoxia: tumorigenesis, angiogenesis, imaging, pseudoprogression, and as a therapeutic target. Jensen RL. *J Neurooncol*. 2009 May;92(3):317-35. Epub 2009 Apr 9. Review.