FACULTY OF MEDICINE AND HEALTH SCIENCES

On Glioblastoma Patient Survival

Surgical, radiological, radiotherapeutic and molecular biological prognostic factors

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Thesis submitted to obtain the degree of
Doctor in Health Sciences
2020 - 2021

GHENT UNIVERSITY

Glioblastoma is the most frequent and most malignant brain tumor. Every year, about 575 new patients are diagnosed with glioblastoma in Belgium. Despite aggressive treatment with chemoradiotherapy after surgery, median overall survival is only 15 months following diagnosis. Prognostic factors are essential to facilitate the shared decision-making process between patient and physician. In this thesis, several prognostic factors for glioblastoma patient survival are critically examined.

Neurosurgical treatment of glioblastoma patients has long sparked intense debate. Nowadays, research has shown that complete resection of the contrast-enhancing part of the tumor results in better survival, if no harm is inflicted to the patient. In this thesis we present evidence that patients may also benefit from less than complete resection, compared to biopsy-taking only.

The subventricular zone (SVZ), a specific region of the brain next to the ventricles, is the largest reservoir of neural stem cells in adults. Growing evidence shows an important relationship between the SVZ and glioblastoma, among other because the malignant stem cell probably resides in the SVZ. Contact of glioblastoma with the SVZ at diagnosis is an independent negative prognostic factor. But contrary to previous reports, our research showed no clear effect of SVZ irradiation on glioblastoma patient survival.

Genetic factors have a crucial role in glioblastoma. In this thesis, an important molecular biological factor was examined: methylation of the promoter of the O^6-methylguanine-DNA-methyltransferase (*MGMT*) gene. MGMT is a DNA-repair enzyme, and if suppressed, the tumor will be more vulnerable to chemoradiotherapy. We showed that methylation of the *MGMT* promoter is not an "all or nothing" phenomenon and, more importantly, that glioblastoma patients with weakly methylated glioblastoma still have significantly better overall survival than patients with unmethylated tumors.

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So, SVZ contact is a negative prognostic factor while resection of glioblastoma, even partially, and methylation of the *MGMT* promoter are both positively correlated with glioblastoma patient survival. Irradiation of the SVZ does not seem a valid treatment option for glioblastoma patients but, in the future, the SVZ may be targeted differently, e.g., by blocking the communication pathways between glioblastoma and the SVZ. Most likely, new methods will be developed to suppress the action of the MGMT enzyme in glioblastoma, e.g., by interacting with small RNA molecules ('micro-RNA').

About the author

Giorgio Hallaert obtained the medical degree in 2003 at Ghent University. He was subsequently selected for the neurosurgical training program and acquired the license to practice neurosurgery in 2009. He currently works at Ghent University Hospital and ZorgSaam Ziekenhuis Terneuzen (the Netherlands). In addition to his general neurosurgical practice, his academic interests are in neuro-oncology (gliomas) but also in health care management and medical ethics.

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Financing

Ghent University Hospital, Center for Oncology
Lux Luka Foundation
Fonds Arne Lannoy, AKA Zorro

We sincerely thank these non-profit organizations for their support of this academic work.

Online Public Doctoral Defense

Friday, August 20, 2021 at 5 pm

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