## **Glioblastoma History**

The first recorded reports of gliomas were given in British scientific reports, by Berns in 1800 and in 1804 by Abernety  $^{1)}$ 

During the early 19th century, glioblastoma was considered of mesenchymal origin and was defined as a sarcoma.

In 1863, Rudolf Ludwig Karl Virchow demonstrated its glial origin<sup>2)</sup>, and in 1914 Mallory proposed the term glioblastoma multiforme. However, it was not until 1925 that Globus and Strass presented a complete description of the neoplasm, at which point the most common term became spongioblastoma multiforme. Finally, in 1926, Percival Bailey and Harvey Cushing successfully reintroduced the term originally proposed by Mallory: glioblastoma multiforme, based on the idea that the tumor originates from primitive precursors of glial cells (glioblasts), and the highly variable appearance due to the presence of necrosis, hemorrhage and cysts (multiform).

In the 1920s, Walter Edward Dandy took a radical step by removing the entire hemisphere of two comatose patients suffering from Glioblastoma. Despite this intervention, these patients ultimately succumbed to the disease, providing the first evidence of how truly invasive Glioblastoma is <sup>3)</sup>.

Between 1934 and 1941 the most prolific researcher in glioma research was Hans-Joachim Scherer.

He made the distinction between primary and secondary Glioblastomas and postulated some of the clinico-morphological aspects of Glioblastoma. With the introduction of molecular and genetic tests the true multifomity of Glioblastoma has been established, with different genotypes bearing the same histomorphological and IHC picture, as well as some of the aspects of gliomagenesis <sup>4</sup>.

In 1976 the International Classification of Diseases for Oncology (ICD-O) was created by the WHO for recording the incidence of malignancy and survival.

In 1993, Glioblastoma was removed from its original category and placed in the spectrum of "Astrocytic Tumours" and is classed as WHO grade IV astrocytoma.

The World Health Organization Classification of Tumors of the Central Nervous System 2007 nomenclature omited "multiforme" <sup>5)</sup>.

While glioblastoma was historically classified as isocitrate dehydrogenase (IDH)-wildtype and IDHmutant groups, the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT-NOW) and the World Health Organization Classification of Tumors of the Central Nervous System 2021 clearly updated the nomenclature to reflect glioblastoma to be compatible with wildtype IDH status only. Therefore, glioblastoma is now defined as "a diffuse, astrocytic glioma that is IDH-wildtype and H3-wildtype and has one or more of the following histological or genetic features: microvascular proliferation, necrosis, TERT promoter mutation, Epidermal growth factor receptor gene amplification, +7/-10 chromosome copy-number changes (CNS WHO grade 4)<sup>6</sup>.

In 2022 although survival has not substantially improved, major advances have been made in our understanding of the underlying biology. It has become clear that these devastating tumors recapitulate features of neurodevelopmental hierarchies which are influenced by the microenvironment. Emerging evidence also highlights a prominent role for injury responses in steering cellular phenotypes and contributing to tumor heterogeneity<sup>7)</sup>

## References

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