

Circulating Tumor Cell (CTC) Analysis for Glioblastoma



Parsortix® technology enables repeatable and minimally invasive access to tumour-derived biomarkers for multiomic analysis.



Glioblastoma (GBM) is the most aggressive brain cancer in adults, and it presents a challenge for longitudinal biomarker testing due to the tumour location and the highly invasive nature of traditional tissue biopsy techniques. ANGLE's Parsortix technology offers a blood-based solution for capturing CTCs, enabling longitudinal genomic, transcriptomic, epigenetic and proteomic profiling of GBM tumour biology.

Blood-based liquid biopsies are already enabling minimally invasive biomarker testing in other cancer types. For GBM, CTCs would provide an alternative for patients who cannot undergo surgical biopsy due to tumour location or health status.

CTCs are a promising solution to help classify patients for selection of targeted therapies & enrollment into clinical trials

Multiple studies have shown that CTCs can be detected in the peripheral blood of a majority of GBM patients—detection rates as high as 77% to 84% have been reported^{1,2}. There are numerous potential applications for CTCs in GBM research and clinical development, including:

Biomarker detection

- Multiomic profiling of CTCs may help classify patients for selection of targeted therapies and enrollment into clinical trials
- The ability to capture and harvest CTCs is especially valuable for biomarker testing in cases where tissue is not available.
- CTC analysis may be complementary to imaging especially in cases of pseudo progression.

Longitudinal monitoring

- Minimally invasive liquid biopsy enables longitudinal monitoring of therapeutic resistance and sensitivity.

Prognosis

- Mesenchymal CTCs are a prominent feature in GBM and their presence and characterisation offer insights into disease progression and treatment resistance in GBM patients³.

ANGLE's Parsortix technology is supported by a growing number of published studies demonstrating potential utility in GBM patient management

- Patented CTC capture method is based on size and deformability—not surface markers—making it particularly suitable for mesenchymal and EMT-transitioning CTCs, which are common in GBM.
- Parsortix technology was used to provide the first evidence of CTC clusters in GBM patient blood samples. The publication by Krol et. al (2018) concluded, "These findings highlight the use of CTCs as a blood-based analyte for non-invasive GBM assessment"⁴.
- Copy number alternation (CNA) analysis of CTCs, isolated from GBM patient blood using Parsortix technology, revealed a novel finding: approximately 51% of CTCs exhibited CNAs, while 49% displayed a wildtype profile⁵. This further emphasises the potential use of CTCs to provide real-time insights into GBM biology and disease progression.

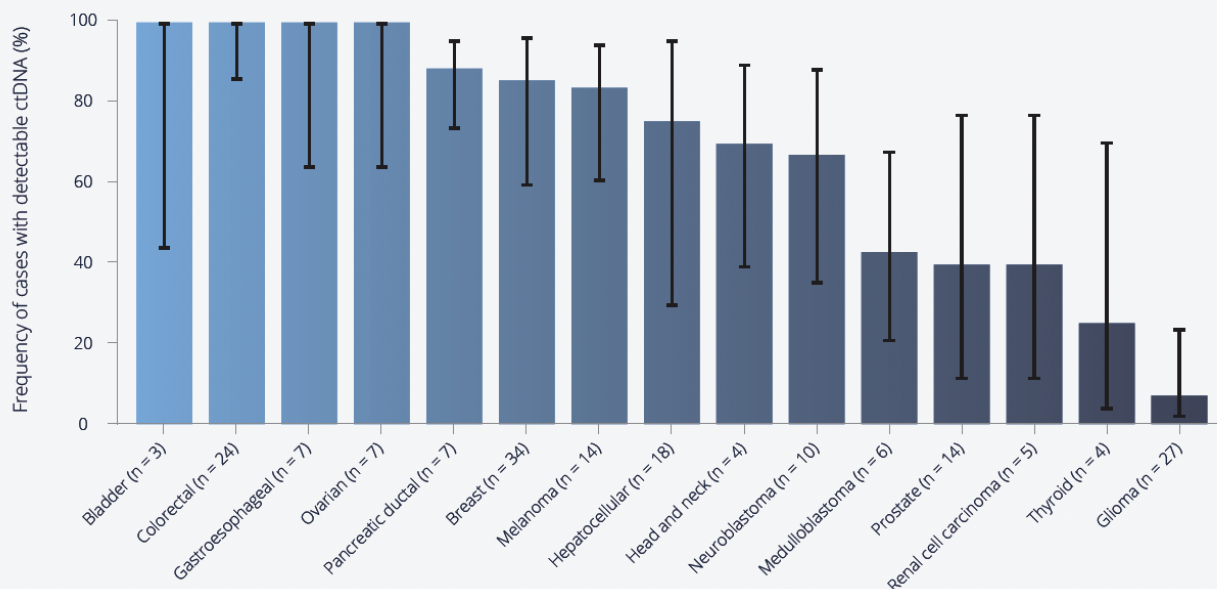
Circulating tumour DNA (ctDNA) is not a viable blood-based analyte in GBM

While **blood-based** ctDNA has shown utility in several cancer types, GBM presents a unique challenge.

A landmark study by Bettegowda et al. (2014) evaluated ctDNA levels in **blood from** over 600 patients across 14 solid tumour types. ctDNA was detected in less than 10% of glioma patients, compared to more than 75% patients with cancers such as colorectal, pancreatic and breast cancer⁶.

This **finding** correlates with **further reports of** low ctDNA concentrations in **glioma patients'** blood, which may be due to the blood-brain barrier (BBB) restricting the passage of many macromolecules from the central nervous system into the peripheral circulation⁷. It is also possible that gliomas, such as GBM, release less ctDNA than other solid tumour types.

These findings underscore a critical limitation of ctDNA for brain tumour liquid biopsy applications and emphasise the need for alternative blood-based analytes.



Bar graph showing the percentage of patients with detectable ctDNA across cancer types. Error bars represent detection range. Glioma had the lowest ctDNA detection rate (<10%). Source: Bettegowda et al., Sci Transl Med, 2014.

In contrast, CTCs are relatively common in GBM

The mechanisms behind the higher detection rate for CTCs in GBM are not fully understood, but several factors are likely to be involved, including:

Physical characteristics

- CTCs are intact, viable tumor cells that may be better equipped to traverse the BBB or enter the circulation during processes such as tumour invasion, angiogenesis, or surgical manipulation^{1,4,8}.

Tumour biology

- GBM cells may have properties (such as stem cell-like features and enhanced motility) that facilitate their entry into blood vessels, even in the presence of the BBB⁸.

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