
# Circulating Tumor Cells in Patients with Glioblastoma

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## Introduction

Glioblastoma (GBM) is characterized by necrosis, angiogenesis, and inevitable recurrence. Despite it's aggressiveness, GBM rarely form extra-cranial metastases suggesting impediments in vascular invasion, survival in circulation or implantation. Advances in microfluidics have successfully identified circulating tumor cells (CTCs) in lung, prostate, and breast cancer patients. Using a novel CTC microfluidic device, we hypothesize that GBM patients have CTCs, which can be captured, quantified, and analyzed for molecular and genetic markers.

## Methods

We developed a microfluidic device (CTC-iChip) capable of capturing CTCs from whole blood via immunomagnetic depletion of hematopoietic blood cells. Using GBM-specific antibodies, we validated our CTC-iChip using GBM cell lines spiked into healthy donor blood. After successfully establishing our device, we evaluated venous blood samples (10 ml) from 6 healthy donors and 33 GBM patients preoperatively and postoperatively including chemotherapy and radiation therapy. CTCs were stained with a cocktail of GBM-specific antibodies and scanned by automated fluorescence microscopy. CTCs and their matched pathological specimens from surgery were further analyzed by Fluorescence in-Situ Hybridization (FISH).

## Results

CTCs were detectable in at least one blood sample in 14/33 (42%) GBM patients. Patients with progressive disease harbored a median 11.8 CTCs per ml (mean 13.6 ± 10.7) compared to 2.1 CTCs per ml (mean: 4.0 ± 2.7) in patients with stable disease. CTC detection was significantly associated with disease progression (p-value: 0.03), but not with other clinical variables such as disease location, extent of resection, or genotype. FISH analysis of CTCs from EGFR-amplified and Chr7-polysomy GBM patients revealed 30/36 (83.3%) CTCs harbored concordant molecular aberrations.

## Conclusions

We identify the first evidence of CTCs in the peripheral blood of GBM patients. CTC frequency often varies during the course of therapy and is correlated with disease progression. Further studies are needed to define this novel discovery and its potential role in the care of GBM patients.

## Learning Objectives

1) Evaluate the role of blood based tests in the detection of glioblastoma.

2) Evaluate the potential for circulating tumor cells to provide information about a patient's disease status.