INTRODUCTION: Glioblastoma (GBM) is the most lethal primary brain tumor with a median survival of 15 months despite resection and concurrent radiochemotherapy. Among the many challenges in treating glioblastoma patients is the ability to differentiate pseudoprogession (PsP) and "radiation necrosis" (RN) from true recurrent GBM (rGBM). While PsP and RN occur in 15% to 30% of glioblastoma treated with concurrent radiochemotherapy, they are difficult to distinguish from recurrent GBM (rGBM) with magnetic resonance imaging (MRI). Thus, despite various MRI grading classifications, biopsy remains the gold standard. We and others have recently identified myeloid-derived suppressor cells (MDSC) in both tumor microenvironment and peripheral blood of GBM patients. Our recent studies also identified the MDSC-related protein VN2 on CD14+ monocytes in various conditions.

METHODS: Fresh peripheral blood was collected per institutional review board-approved protocol and monocytes isolated by density gradient centrifugation. CD14+ were then isolated using magnetic CD14 micro beads. HLA-DR- and/or VN2+ cells were quantitated using multicolor flow cytometry with isotype-matched antibody controls. Analysis was performed using Winlist software; statistical significance was determined using Student t test.

RESULTS: Median MDSC (CD14+ HLA-DR-) comprised 52% of monocytes in peripheral blood of GBM patients (n = 12) but only 4% to 5% of patients with PsP, RN or normal controls (n = 5 and n = 11 respectively; P < .001). Conversely, CD14+VN2+ monocytes were found in 26% of patients with verified RN (n = 5), while the level in rGBM and normal controls was 8% and 12% (n = 12 and n = 11 respectively; P < .001). Together, MDSC and VN2 were 100% sensitive and 100% specific in differentiating rGBM from PsP and RN in our retrospective studies of 16 patients.

CONCLUSION: This novel, quick and inexpensive liquid biopsy performed on peripheral blood could replace invasive brain biopsy if preliminary results are confirmed in prospective studies currently underway.