

VALIDATION OF THE RANO CRITERIA FOR QUANTIFYING THERAPEUTIC RESPONSE OF HUMAN BRAIN TUMORS USING COMPUTER ASSISTED MEDICAL DIAGNOSIS (CAMD) TECHNOLOGY

Simon Salinas¹, Steve Lau², Kate Drummond³, Christen Barras², Pramit Phal^{1,2}, Patricia Desmond^{1,2}, and Bradford Moffat¹

¹The University of Melbourne, Melbourne, Victoria, Australia, ²Radiology, Royal Melbourne Hospital, Melbourne, Victoria, Australia, ³Neurosurgery, The University of Melbourne, Melbourne, Victoria, Australia

TARGET AUDIENCE: Neuroradiologists, neurooncologists, radiation oncologists, neurosurgeons or anyone involved with brain tumour response therapies.

PURPOSE: We have created a novel CAMD tool to enable streamlined clinical application of the **Response Assessment in Neuro-Oncology (RANO) criteria** to measure brain tumor radiological response.

The **RANO criteria** are the standard criteria [1,2] for quantifying therapeutic response in brain tumour patients. However, implementation is problematic because of the requirements to longitudinally record two-dimensional measurements on up to ten lesions and applying a strict set of rules for response assessment. In addition, there is still a need for validation before the criteria could be applied clinically or utilized as a surrogate biomarker in clinical trials [4].

The aims of this study were to quantify the efficiency of making RANO assessments using an open source CAMD graphical user interface and to correlate them with clinical outcome in glioblastoma patients undergoing chemo and radiation therapy.

METHODS: MRI scans from 31 newly diagnosed glioblastoma (WHO grade IV) patients were reviewed by four experienced reviewers. A baseline pre-treatment MRI study and a post-treatment (12 weeks to avoid pseudo-progression) MRI study were compared to assess response based on the RANO criteria, categorizing to either stable disease (SD) or progressive disease (PD). This assessment was performed using a CAMD graphical user interface developed in MatLab [3] that allowed reviewers to easily draw sets of perpendicular lines, visualize volumetric response and automatically derive the RANO criteria.

The individual times spent per case were recorded. Median survival times of the SD and PD groups were compared using a Log-rank (Mantel-Cox) test.

RESULTS: The CAMD interface (Fig. 1) provided an excellent user friendly and efficient environment to assess the RANO criteria for all 31 patients. The average time for RANO assessment was 6.4 minutes (4.8 std. dev). The median survival of the SD patients (Fig. 2) was 105 weeks, which was significantly ($p=0.04$) longer than that of the PD patients (64 weeks). The Hazard Ratio (logrank) obtained was 2.426 with a 95% CI of 1.104 to 9.332.

DISCUSSION: The RANO criteria are currently the standard method for assessing radiological response in glioblastoma patients however it, is seldom used clinically, is costly and laborious to use in clinical trials and is yet to be validated. The CAMD interface developed in this study allows the criteria to be efficiently assessed in less than 10 minutes per patient. The results of the study validate the use of the RANO criteria 3 months post treatment whereby SD patients have been shown to have a median 41-week survival advantage over PD patients.

CONCLUSION: In conclusion the RANO criteria can be assessed efficiently when using CAMD technology and is valid for quantification of therapeutic efficacy in glioblastoma patients. The open source CAMD interface used in this study will be readily updated to also include other experimental imaging biomarkers such as functional diffusion [5] and parametric response mapping [6].

REFERENCES:

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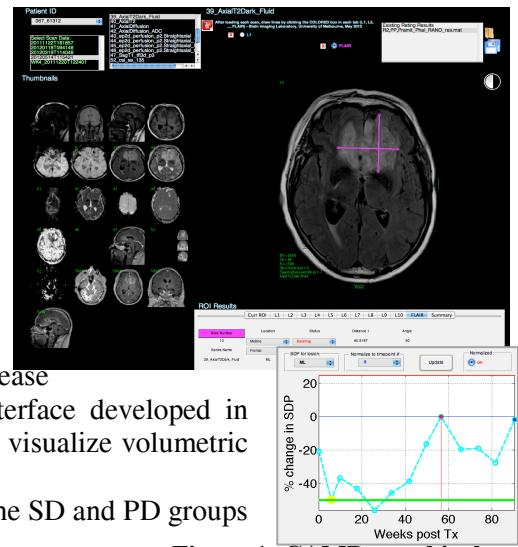


Figure 1: CAMD graphical user interface

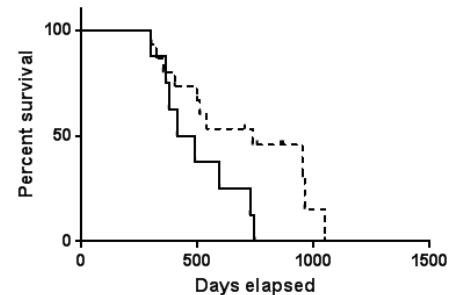


Figure 2: Survival analysis (SD - dashed lines, PD - solid lines)