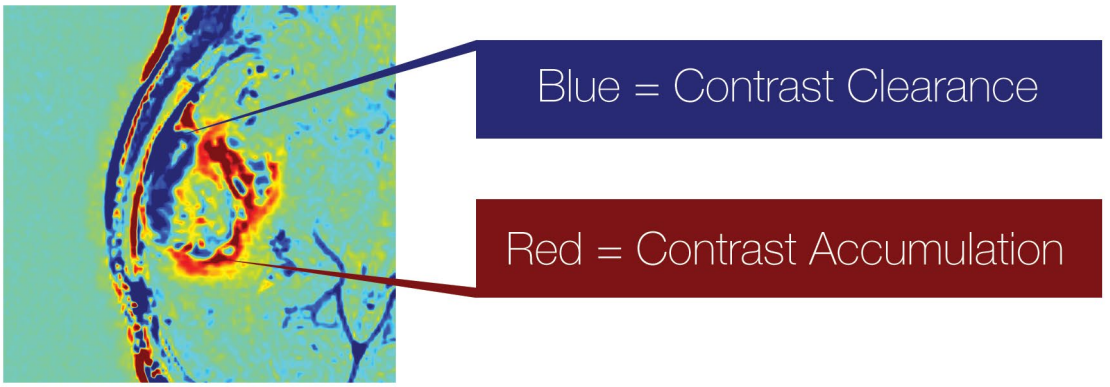
BRAINLAB

DECISION MAKING WITH TRAMs

Treatment Response Assessment Maps

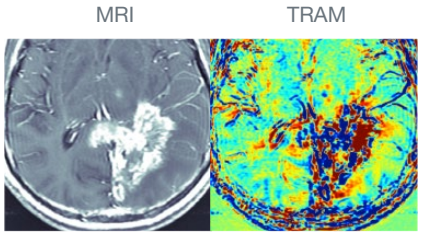


Treatment Response Assessment Maps (TRAMs) is a novel MRI-based methodology for the high resolution depiction of tumor and non-tumoral tissues in brain tumor patients. Elements TRAMs* differentiate between contrast clearance and accumulation and support clinicians in separating tumor progression and treatment effects, such as radiation necrosis. Clinical studies affirm high positive predictive values (PPV) and outstanding sensitivity to active tumor.

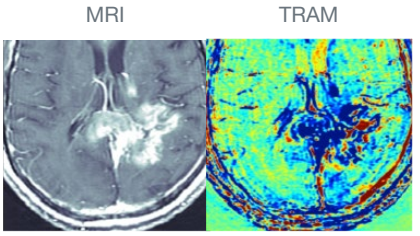
Developed at Sheba Medical Center, Tel Aviv, with technology provided by Brainlab, Elements TRAMs serve clinical specialties including Radiosurgery, Radiation Oncology, Neurosurgery, Neuro Oncology and Neuroradiology.

CLINICAL USE

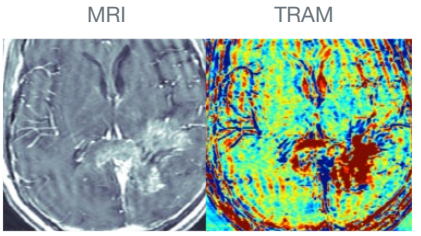
- High resolution differentiation between contrast clearance and accumulation
- Histological validation confirms strong positive predictive values and sensitivity for active tumor tissues of most known brain tumor types
- Supports ongoing assessment and clinical decision making before, during and after most treatments as the calculated color distribution is normalized and with that directly comparable over time



Baseline



Progression under treatment #1: TRAMs indicate progression in blue after initial treatment



Response to treatment #2: TRAMs depict response after adapted treatment

METHODOLOGY

- Two acquisitions of standard T1-weighted MRI—once 5 minutes and again 60-105 minutes after injection of a standard dose of contrast agent
- First series is intelligently subtracted from the second, resulting in the TRAMs
- TRAMs are high resolution, volumetric maps separating regions of contrast clearance (blue) from contrast accumulation (red) more than one hour post contrast injection
- Tumor tissues present efficient contrast clearance due to their viable vessels thus are depicted in blue, while non-tumor tissue with less efficient clearance are depicted in red

*Works in progress.

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CLINICAL VALIDATION PERFORMED AT SHEBA MEDICAL CENTER, TEL AVIV, ISRAEL

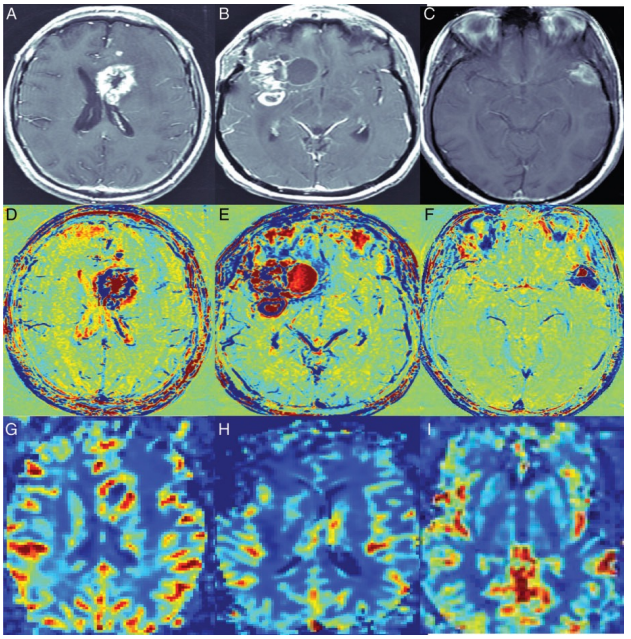
Delayed contrast extravasation MRI: a new paradigm in neuro-oncology, *Zach et al, Neuro Oncology, 2015*

Background. Conventional MRI is unable to differentiate tumor/non-tumor enhancing tissues. The Sheba group has applied delayed-contrast MRI for calculating high resolution Treatment Response Assessment Maps (TRAMs) clearly differentiating tumor/non-tumor tissues in brain tumor patients.

Methods. One hundred and fifty patients with primary/metastatic tumors were recruited and scanned by delayed-contrast MRI. Of those, 47 patients underwent resection during their participation in the study. Region of interest/threshold analysis was performed on the TRAMs and correlation with histology was studied.

Results. Histological validation confirmed that regions of contrast agent clearance in the TRAMs >1 h post contrast injection represent active tumor, while regions of contrast accumulation represent non-tumor tissues with 100% sensitivity and 92% positive predictive value to active tumor. Significant correlation was found between tumor burden in the TRAMs and histology in a subgroup of lesions resected en bloc (r^2 = 0.90, P<.0001). The feasibility of applying the TRAMs for differentiating progression from treatment effects, depicting tumor within hemorrhages, and detecting residual tumor post-surgery was demonstrated.

Conclusions. The TRAMs present a novel model-independent approach providing efficient separation between tumor/non-tumor tissues by adding a short MRI scan >1 h post contrast injection. The methodology uses robust acquisition sequences, providing high resolution and easy to interpret maps with minimal sensitivity to susceptibility artifacts. The presented results provide histological validation of the TRAMs and demonstrate their potential contribution to the management of brain tumor patients.



Contrast-enhanced MRI (A–C), the calculated TRAMs (D–F), and rCBV maps (G–I) of GBM patients 3 weeks (A, D, and G) and 3 months (B, E, and H) postchemoradiation and a patient with a malignant melanoma brain metastasis (C, F, and I) 2 months post stereotactic radiosurgery. The 3 lesions, all showing a blue/tumor component in the TRAMs, were categorized by the study neuroradiologist as having high (G), moderate (H), and low rCBV (I).

Sources:
Leor Zach, David Guez, David Last, Dianne Daniels, Yuval Grober, Ouzi Nissim, Chen Hoffmann, Dvora Nass, Alisa Talianski, Roberto Spiegelmann, Galia Tsarfaty, Sharona Salomon, Moshe Hadani, Andrew Kanner, Deborah T. Blumenthal, Felix Bukstein, Michal Yalon, Jacob Zauberman, Jonathan Roth, Yigal Shoshan, Evgeniya Fridman, Marc Wygoda, Dror Limon, Tzahala Tzuk, Zvi R. Cohen, and Yael Mardor. Delayed contrast extravasation MRI: a new paradigm in neuro-oncology, Neuro Oncol. 2015 Mar;17(3):457-65

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