A generalized method for detecting therapy-induced leukoencephalopathy

J. O. Glass[1], C-H. Pui[2], W. E. Reddick[1]

[1]Radiological Sciences, St. Jude Children's Res Hosp, Memphis, TN, United States, [2]Hematology/Oncology, St. Jude Children's Res Hosp, Memphis, TN, United States

Purpose: Reliably detecting subtle therapy-induced leukoencephalopathy, a hyperintensity of white matter on T2 and FLAIR imaging, in children treated for cancer is a challenging task due to its nearly identical MR properties and location with unmyelinated white matter. Previous work presented a methodology based on differences in signal intensity. The current study extends the previous work by adding a gradient magnitude threshold to reduce false positives and by creating a more generalized approach based on quantitative T1 (qT1) and T2 (qT2) relaxation changes.

Methods: All MR imaging was performed without contrast on a 1.5-T Vision (Siemens Medical Systems, Iselin, NJ) whole-body imager. Patients underwent a clinical imaging protocol after informed consent had been obtained from the patient, parent, or guardian, as appropriate. MR imaging sets included T1-weighted (TR/TE/TI = 8000/29/300 ms), PD- and T2-weighted (TR/TE1/TE2 = 3500/17/102 ms), and FLAIR (TR/TE/TI = 9000/119/2470 ms) sequences. The qT1 was computed from a turbo inversion recovery imaging sequence (TR/TE/TI = 2500/29/100,500,900,2389 ms), and the qT2 from a turbo spin-echo sequence (TR/TE = 2000/22.5-360 ms, 16 echoes).

Imaging, near the start of therapy for ALL, was collected for 44 children aged 1.7-18.7 (median 5.9) years. All subjects had received at least one course of high-dose methotrexate (HDMTX >1g/m^2). MR imaging sets were registered and RF corrected. A combined imaging set consisting of T1, T2, PD, and FLAIR MR images and white matter, gray matter and CSF apriori maps from a spatially normalized atlas were then analyzed with a neural network segmentation based on a Kohonen Self-Organizing Map (SOM).[1,2] To improve the differentiation between true abnormal regions and CSF contaminated regions with high FLAIR signal, an in-plane gradient magnitude threshold was added to the segmentation algorithm[3]. Segmented maps were then manually classified to identify the most hyperintense region and the normal appearing genu region. A difference measure was then computed within each patient for both signal intensity (T2 and FLAIR) and quantitative relaxation measures (qT1 and qT2). After establishing a difference threshold condition with the signal intensity to distinguish therapy-induced leukoencephalopathy from assumed normal unmyelinated white matter on the first examination (similar to the previous study), three additional subsequent examinations on each patient were investigated. These examinations occurred after 3 courses of HDMTX, after all 7 courses of HDMTX and approximately 90 weeks post the last course of HDMTX. Regression analyses were then used to map signal intensity of the T2 and FLAIR images to qT1 and qT2 relaxation rates for the same regions. These regression equations were then used to establish qT1 and qT2 thresholds.

Results and Discussions: Analysis of the distributions of the signal intensity differences revealed two distinct groups in the first examination (Figure 1). A threshold with the improved segmentation algorithm was established for both FLAIR (change $\geq$ 136) and T2 (change $\geq$ 196). Comparing these divisions to the radiologist report revealed an accuracy of 79% with a sensitivity of 81% and specificity of 76%, results that are very similar to those reported with the previous technique. The thresholds from the signal intensity based approach were then used to produce thresholds for both qT1 (change $\geq$ 116 ms) and qT2 (change $\geq$ 25 ms). The distinctions between the group assumed as normal unmyelinated white matter and the group assumed to be leukoencephalopathy is more apparent using the quantitative imaging thresholds (Figure 2). As expected, comparing the relaxation thresholds to the radiologist reports revealed similar accuracy (79%), sensitivity (84%) and specificity (74%) to the signal intensity based method. This new method based on relative differences in quantitative relaxation measures is more generalized for implementation across institutions and imaging equipment at the same field strength.

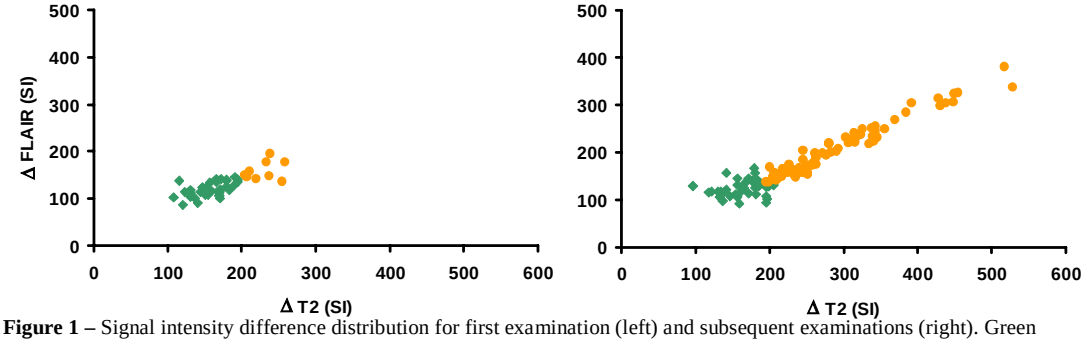

Figure 1 – Signal intensity difference distribution for first examination (left) and subsequent examinations (right). Green diamonds are assumed normal and orange circles are assumed abnormal.

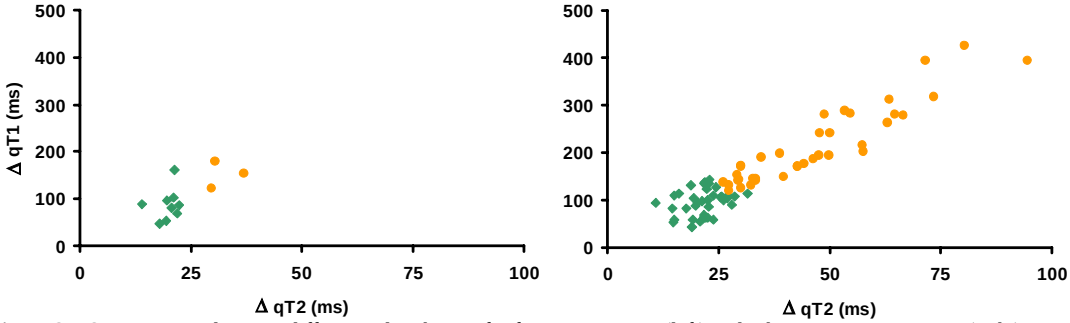

Figure 2 – Quantitative relaxation difference distribution for first examination (left) and subsequent examinations (right). Green diamonds are assumed normal and orange circles are assumed abnormal.

Conclusion: Subtle therapy-induced leukoencephalopathy can be reliably and reproducibly detected even in young children treated for cancer using this generalized approach based on relative differences in quantitative relaxation measures.

References: 1. Reddick WE, IEEE-TMI 16:911, 1997. 2. Reddick WE, MRM 47:912, 2002. 3. Glass JO, ISMRM 602, 2003.