Use of Lesion Walker Classification in Patients with Multiple Sclerosis

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Objective: Develop software with a well-defined ontological scheme for the classification of multiple sclerosis (MS) lesion evolution on serial MRI scans which enables automatic classification together with operator verification and modification.

Background: MS lesion activity is often tracked over a period of time and classified accordingly. Classification typically occurs after an operator has drawn regions of interest (ROIs) delineating the lesions, which enables the easy calculation of lesion volume. As an example, a lesion would be classified as "Stable" if there were no significant change in volume from the previous scan, or classified as "Increasing" if it increased in volume. Some cases are potentially difficult to classify such as: 1) where two or more lesion have merged, 2) where lesions have separated from other lesions, or 3) where an operator may not have contoured a lesion on a given scan.

Methods:

Lesion Complex: We define a lesion to be a distinct connected region of masking voxels determined from a binary lesion mask created for a single scan. We also define a new term: the "lesion complex" (LC). To determine a LC, one must first form the union of all serial binary lesion masks and determine the resulting distinct connected regions. A LC on a particular scan is then defined as any collection of masking voxels from the scan's lesion mask that are in the same connected region in the union of all lesion masks. If the LC is the set of voxels from a single or multiple lesions at a given time; we term the LC as existing or "present". If there are no voxels meeting this condition, then we term the LC as "not present" for that scan, as would be the case for a lesion that "Disappeared". We will use the term LC in the same context as lesion, and use it both in the context of an individual scan, and as entity that is tracked over time.

Our classification scheme for LCs has the advantage that a LC at a given time point maps to exactly one LC at every other time point. Based on the "presence" and/or volume of the LC, both currently and previously, one of the following labels can be uniquely applied to the current instance: Baseline, Pre-Lesion, Stable, Newly Disappeared, Previously Disappeared, Recurrent, Newly Increasing, Persistently Increasing, New, and Resolving. These labels allow for several grammatical consistency checks. For instance, the Pre-Lesion label, which is only used to denote that a LC is not present currently or previously, can only be preceded by the Pre-Lesion label, and immediately followed by the label Pre-Lesion or New. A LC is classified as increasing/decreasing if its volume increases/decreases more than a relative threshold. The threshold is set at 70% for small lesions ($\leq$65ml) and linearly decreases to 15%, for absolute changes $\geq$100ml.

Missing ROIs: If a lesion ROI was not drawn on a scan due to operator error, but was marked as present on a previous or subsequent scan, two problems arise. Firstly, it would be labeled as "Disappeared", which is not correct. Secondly, when the ROI is drawn again on a later scan, it would be incorrectly labeled as "Recurrent". As a quality control step, a "missing ROI" program was developed to track LCs and locates where a LC was not contoured on a scan slice at one time point, but was contoured on the equivalent scan slice at another time point. The output is a Java Image Manipulation (JIM) format ROI file which can be rapidly examined by an expert to determine if the lesion ROI was missing due to operator error, or if the ROI should truly not be drawn.

The framework provided by the definition of the LC, together with the quality control step of checking for missing ROIs, allows the classifications of the LCs to be generated automatically and verified efficiently using a "Lesion Walker" program. This program displays the ROIs associated with a given LC across all scans. The operator is then free to accept or modify the proposed LC classifications provided by the program (see Figure 1). After a LC is labeled for all time points, the program steps (or walks) to the next LC and displays the lesion contours for it. The program continues in this manner until all LCs have been labeled.

Program Testing: The programs were tested on data sets from 5 subjects, each with 4 serial FLAIR MRI scans which had been spatially realigned. Lesion ROIs were drawn using JIM4. The Lesion Walker program was assessed on the basis of operator calculation time and the label classification agreement between the program and the operator.

Results: The time needed to classify a series of scans using the Lesion Walker program was under 20 minutes for all cases. The classification scheme agreed with operator classifications in greater than 95% of the classifications.

Conclusion: The Lesion Walker and Missing ROI programs: 1) reduce operator analysis time, 2) improve analysis rigor with the addition of a defined quality assurance check, 3) provide a high initial agreement level with an operator's classifications, and 4) provides the operator with the ultimate analysis control, by allowing easy reclassifications that are consistent with the labeling relationships. By comparison, a traditional lesion activity analysis requires several hours, becomes exponentially more difficult as more scans are added, and is highly subjective. Finally, a traditional analysis is not well-defined in cases of lesions separating or merging. Knowing that the analysis went through a forced quality control step gives higher credence to the results.

Figure 1: Example of Lesion Walker Program: Displaying a LC with ROIs on 2 slices across 4 serial FLAIR scans. The program proposed sequential LC labels of: Baseline, Stable, Stable, and Stable.