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Assessing Disability in Multiple Sclerosis Patients from the Measurement of the Spatial Dispersion of the Lesion Load

A. Pinti[1,4], B. Lenne[2], L. Peyrodie[3], E. Watelain[4,5], P. Hédoux[6], H. Toumi[1]

[1]IPROS - EA 4708 I3MTO, CHRO - 1 rue Porte Madeleine - BP 2439 - 45032 Orléans, France
[2]Groupe Hospitalier de l'Institut Catholique de Lille, 59462 Lomme, France
[3] Hautes Etudes d'Ingénieur, Lille 59046, France
[4]Univ. Lille Nord de France, UVHC, 59313 Valenciennes, France
[5] HandiBio, EA 4322, Université du Sud Toulon-Var, 83957 La Garde, France
[6]SSII ACFY, 92ter rue Roger Salengro, 59300 Famars, France
(antonio.pinti@univ-valenciennes.fr; Lenne.Bruno@ghicl.net; laurent.peyrodie@hei.fr; eric.watelain@univ-valenciennes.fr;phedoux@yahoo.fr; hechmi.toumi@univ-orleans.fr)

Abstract:

In this article, we examine the relationship between the spatial dispersion of lesion load and disability score in patients with Multiple Sclerosis (MS). From the 3D spatial location of brain lesions, four measures are considered:

- Measure of compactness;
- Volume ratio of brain atrophy;
- Euclidean distance determined from the centre of gravity of the brain and the centres of gravity loads lesion;
- Euclidean distance between the pairs of loads lesion.

This study was conducted on 10 MS patients with an EDSS score (Expanded Disability Status Scale) calculated by an expert. Lesion loads are segmented from recordings of Magnetic Resonance Imaging (MRI) by a semi-automatic variational method.

A statistical analysis of the regression between the values of spatial dispersions and EDSS scores was performed. The results show that for patients with similar lesion loads, greater dispersion damage will tend to be linked with a greater degree of disability.

Résumé :

Dans cet article, la relation entre la dispersion spatiale de la charge lésionnelle et un score de handicap chez des patients atteints de Sclérose En Plaques (SEP) est étudiée.

A partir de la localisation spatiale tridimensionnelle des lésions cérébrales, 4 mesures sont réalisées :

- mesure de compacité ;
- rapport volumique de l'atrophie cérébrale ;
- distances euclidiennes entre le centre de gravité du cerveau et ceux des charges lésionnelles ;
- distances euclidiennes entre les paires de charges lésionnelles.

Cette étude est réalisée sur 10 patients ayant un score EDSS (Echelle de cotation clinique du handicap) calculé par un expert. Les charges lésionnelles sont segmentées à partir d'enregistrements d'Imagerie par Résonance Magnétique (IRM) par une méthode variationnelle semi-automatique.

Une analyse statistique entre les valeurs de dispersions spatiales et le score EDSS a été réalisée. Les résultats montrent qu'à charges lésionnelles similaires, une plus grande dispersion des lésions tendra à augmenter le handicap.

Keywords: MS, Segmentation, EDSS, Evaluation.
Mots clés : SEP, Segmentation, EDSS, Evaluation.

1. Introduction

Multiple Sclerosis (MS) for 2000-3000 new cases per year in France and 80,000 people are infected with a steady increase in both the incidence and prevalence [1]. It is the chronic progressive disabling neurological condition most common in young adults [2]. It is characterized anatomically by the successive appearance of foci of demyelination scattered throughout the white matter of the central nervous system (CNS) (brain and spinal cord), in which there has been a plate destruction of the myelin sheath and the axons of neurons. The pathological diagnosis of MS is based on the presence of inflammatory demyelinating plaques scattered in different parts of the CNS and succeeding in time. The temporo-spatial dissemination of lesions in the white matter predominates. [3] The measurement of the total volume of white matter lesions on magnetic resonance images (MRI) is widely used to monitor lesion load and progression of pathophysiological processes in Multiple Sclerosis (MS) [4]. However, previous studies on the volume of T2 images showed that the relationship between lesion volume and the inability of the patient is generally low [5].

In particular, the cross-correlation between the calculated lesion volume in patients on T2-weighted MRI and disability scale (EDSS) [6], is generally between 0.15 and 0.4 with some studies reporting values as higher than 0.6 [5]. A number of factors are known to affect the correlation, including the lack of specificity of imaging pathological T2, reorganization and cerebral plasticity allowing adaptation to local trauma, and limitations of the EDSS [7].

In addition to having limited predictive value, the emphasis on overall lesion load and other factors associated are left unexplored. In this paper, we study mathematical measures of the spatial 3D lesions as predictor of disability of the patient, regardless of lesion volume loads.

Studies have explored the contribution of lesion load [8, 9] consecutive disability of MS, most often based on a probability map of the lesion load [10, 11].

Other studies have explored the quantification of the spatial distribution of demyelinating lesions and their contributions to the disability [9].

We use the term dispersion to define the spatial extent of brain damage.

We hypothesize an impact on the importance of the dispersion of the lesion load on the handicap. Thus, if two patients have the same lesion load, with the greater dispersion of this lesion load would tend to have greater disability due to the greater impact on overall brain activity. This dispersion results in a more diffuse cerebral disconnection, reducing resilience and brain plasticity. The impact of such a disconnection to the brain has been demonstrated in cognitive tasks [12, 13]. From MS patients, recent studies seem to emphasize that the achievement of large networks of myelinated fibres, associated with cortical lesions appear to be major factors contributing to cognitive and behavioral disturbances in MS [13, 14].

The exploration of spatial relations can improve the understanding of the pathological process of MS scalable and potentially lead to the discovery of new markers that could help to evaluate the disability caused by the disease, and to understand the evolution of the disease.

In this article, we examine four measures of dispersion lesion load. These measures are 1) compactness, 2) a report of atrophy brain lesions 3) some distance from a central point and 4) the distance between pairs of lesions.

After calculating each measure for the 10 patients, we perform a statistical analysis to determine the correlation of this data with the Expended Disability Status Scale (EDSS) patients.

2. Method

2.1 Data Sets

The image dataset used within this paper was conducted at the hospital Saint Philibert (Lomme). It focuses on 10 patients. The acquisition protocols of medical images are: T1 FLAIR (TE = 150, TR = 9600, TI = 2200), T2 (TE = 150, TR = 10000, TI = 2200), T1Gadolinium (TE = 150, TR = 10000, TI = 2200), T2 FLAIR (TE = 150, TR = 10000, TI = 2200), voxel size 0.47 * 0.47 * 3.3 mm^3). Images are encoded 12 bits/pixel. Despite its low resolution in z and that the flow artifacts

are particularly visible, T2 FLAIR is essential for the detection of MS lesions, the contrast is excellent on MRI sequences. However, it provides an over-segmentation of lesions and may be used only for MS. This is why we also merged the other terms of T2, T1, T1 Gadolinium to improve segmentation.

2.2 Measures of lesions dispersion

To reflect natural variations in brain size among different patients, we apply the principal component analysis for brain voxels to calculate the anterior-posterior, left-right and upper lower for each patient. The maximum extent along each direction is then used to normalize the distances lesions along the same direction:

$$d(x_r, y_r, z_r) = \sqrt{\frac{d_x^2}{x_b} + \frac{d_y^2}{y_b} + \frac{d_z^2}{z_b}}$$

where: (x_l, y_l, z_l) are the coordinates of voxel lesion;

(x_r, y_r, z_r) are the coordinates of the reference point;

and (x_b, y_b, z_b) are the coordinates of the central point of the brain.

2.2.1 Compacity

Bribiesca developed in [15] to quantify the connectivity forms composed of voxels, compactness is defined mathematically as follows:

$$C \approx \frac{6n - Surface}{6n - \left(\sqrt{n}\right)^3}$$

where *Surface* is the total area of the faces of the solid and is the total number of voxels.

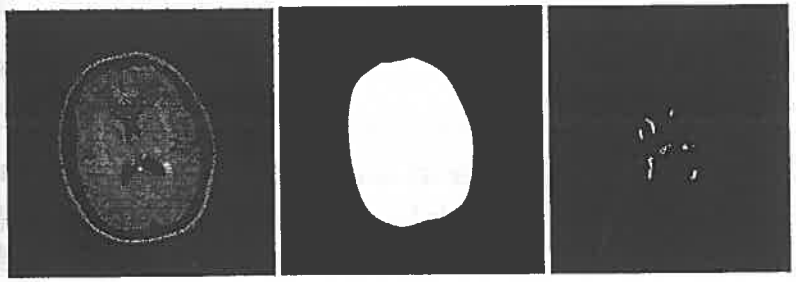
Intuitively, when a form becomes less compact, there are fewer connections between voxels, so the increases and decreases. The main advantages of compactness are: ease of calculation voxels between 0 and 1, which eliminates the need for standardization (Figure 1).

a) MRI Slice b) Compacity map

Figure 1. Compactness measure of brain volume (black spots are associated with MS)

2.2.2 Ratio of the volume of the convex hull and the volume of the brain

For each patient, we compute the convex hull that contains all of the voxels then we use the ratio of the volume of convex hull damage to the brain as a measure of the dispersion. The principle behind this measure is that the use of lesions to form a convex hull defines a region that is most likely to be affected by lesions visible regions outside the convex hull. The volume of the brain acts as a normalization factor (Figure 2).



-a- -b- -c-

Figure 2. Volume measurement of the convex hull and brain volume

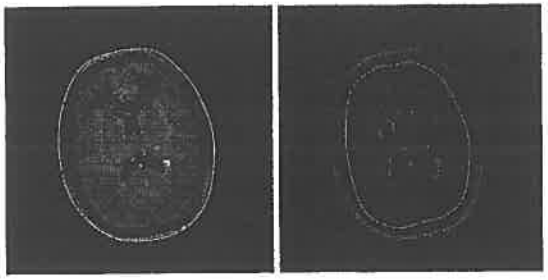
(a) Image MRI T2 (b) Envelope calculated from the thresholded map of compactness

(c) Lesions segmented by active contours [16]

2.2.3 Euclidean distance with respect to a reference point

In order to quantify the dispersion lesions using distances, we calculate the mean, variance, entropy and the asymmetry of the distribution of the Euclidean distance between each voxel and a

lesion fixed reference point. The mean and variance are calculated directly from the distance, while the entropy and asymmetry are calculated from a histogram of distances. We tested a number of different points of reference for our measure, including the centre of gravity of the brain at several extremal points. We observe that the results are dependent on the location of the reference and the focal point of the brain set on the largest slice, but projected onto the slice lowermost gives the highest correlation with the EDSS scale (Figure 3).

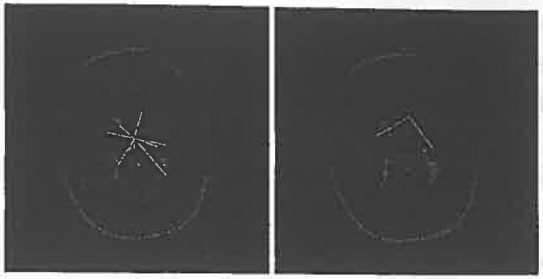


-a- -b-

Figure 3. Segmentation with respect to the interior compactness
(a) Amount calculated out from the map of compactness, the contour is drawn on the map thresholded compactness (b) Envelope inside calculated from the map of compactness and segmentation of MS.

2.2.4 Pair of Euclidean distances

For distance measurement independent of all reference points, we compute the pairwise Euclidean distances for each patient lesion voxels. We measure the mean, variance, entropy and the asymmetry of the distribution of distances in pairs. The mean and variance are calculated from the distances, whereas the entropy and asymmetry are calculated from a histogram of distances. Distances are normalized for each patient (Figure 4) [17].



-a- -b-

Figure 4. Measuring distances of the pairs of the lesion.
(a) Calculation of distances from the centre (x_b, y_b, z_b) of the brain (b) Initialization of arbitrary first point for the calculation of distances pairs, each pair is calculated from the two close distances

2.3 Statistical analysis

The statistical analysis is to determine the relationship between the dispersion of the lesions, the score of the EDSS and brain atrophy in patients. We use regression analysis to determine the presence of a relationship between dispersion of the filler lesion patients and the EDSS score, regardless of brain atrophy [5, 18].

3. Results

3.1 Compacity

To quantify the relationship between compactness and EDSS we calculate the correlations between the compactness and the EDSS score ($r = 0.45$, $p = 0.01$). Pearson correlation between EDSS score and compactness is significant and comparable to that between the EDSS score and volume and shows that patients with less compactness tend to have more disability.

3.2 Convex ratio of the brain volume

The report of the convex hull of the brain volume is correlated with the EDSS score ($r = 0.47$, $p=0.01$).

3.3 Euclidean distance from a fixed reference point

The results show that the values of Euclidean Distance (ED) are significantly correlated with EDSS ($r = 0.50$, $p = 0.001$).

3.4 Pair of Pair-D Euclidean distances

Pair of Pair-D Euclidean distances are correlated with EDSS ($r = 0.47$, $p = 0.01$).

4. Conclusion

In this study, we calculated the spatial dispersion of lesions on MRI of 10 patients with MS using different measures. By linking with the thesis dispersions index values of EDSS and brain atrophy, we found there was a significant correlation between the EDSS scores and measures of dispersion. To quantify the dispersion of the lesions, we used a connectivity based on compactness, the ratio of the convex hull, and two measures based on distance. In this data set, we observed that the distance factor (ED) played a more significant role in relation to the size and connectivity of the convex region. In particular, the variance of the Euclidean distance from a fixed point provides new information on the severity of MS. It can be more sensitive than the total volume of the lesion. From preliminary thesis results, we can conclude that the dispersion measures of lesion load in MS patients may provide new clues for the assessment and prediction of disability.

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