Consiglio Nazionale delle Ricerche
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An Ontological Approach to Classify Potential Lesion in Patients with Multiple Sclerosis

G. De Pietro – A. Esposito

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Abstract

Multiple Sclerosis is a disease of central nervous system, characterized by the development of lesions. In this paper we analyze an algorithm for automatic segmentation of brain tissues and for recognition of sclerosis lesions in intracranial compartments from quantitative evaluations of brain MR studies . An alternative method for lesions individuation, founded on ontological approach, is also presented : from the development of ontology and rules , to the application to a real case with the analysis of results.

1 Introduction

Multiple Sclerosis (MS) is a chronic, inflammatory disease that affects the central nervous system and brings to gradual disability. It's an autoimmune disease, which causes gradual destruction of myelin, a matter that surrounds and protects nerve fibres. The damage brought by attack of myelin sheath leaves multiple scars (*lesions* or *plaques*). Plaques cause interference in the communication between the brain and the rest of the body. In section brain is composed *grey matter* (GM) and *white matter* (WM) and *liquor* (also called *cerebrospinal fluid*): the first one is distributed periferically and constitutes the cerebral cortex; the second one, composed of nerve fibres, is in the centre of the brain and has nuclei of grey matter that are important nervous centres, called *basal ganglia*; the last is a fluid which fills cerebral ventricular cavities and occupies the space between the skull and the cerebral cortex [2].

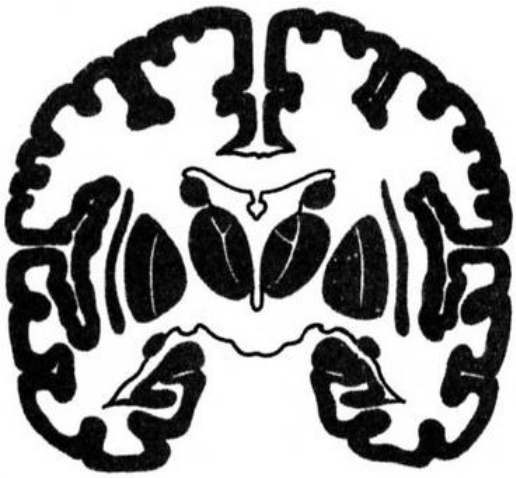

Figure 1 – Placement of grey matter and white matter

When we talk about Multiple Sclerosis , we say WM lesions because they are surrounded by white matter.
In this paper we want illustrate an ontological method with the purpose of recognizing lesions through rules based on lesions features.
The starting point of our work has been an algorithm [1] which realizes automatic segmentation of brain tissues and recognition of white matter lesions, typical of diseases such as multiple sclerosis, from QMCI[1] images.

2 Outline of automatic segmentation algorithm

An element of the algorithm for automatic segmentation of tissue and lesion recognition is the procedure for the classification of WM lesions. This procedure has been replaced using a new approach, with ontology and rules, for lesions identification.

The procedure for the classification of WM lesions used in the algorithm is described in the figure 2 with a flow chart:

[1] QMCI is a technique designed to combine multiparametric MR information in a single colour coded image, where each MR parameter is displayed as a chromatic component of the image.

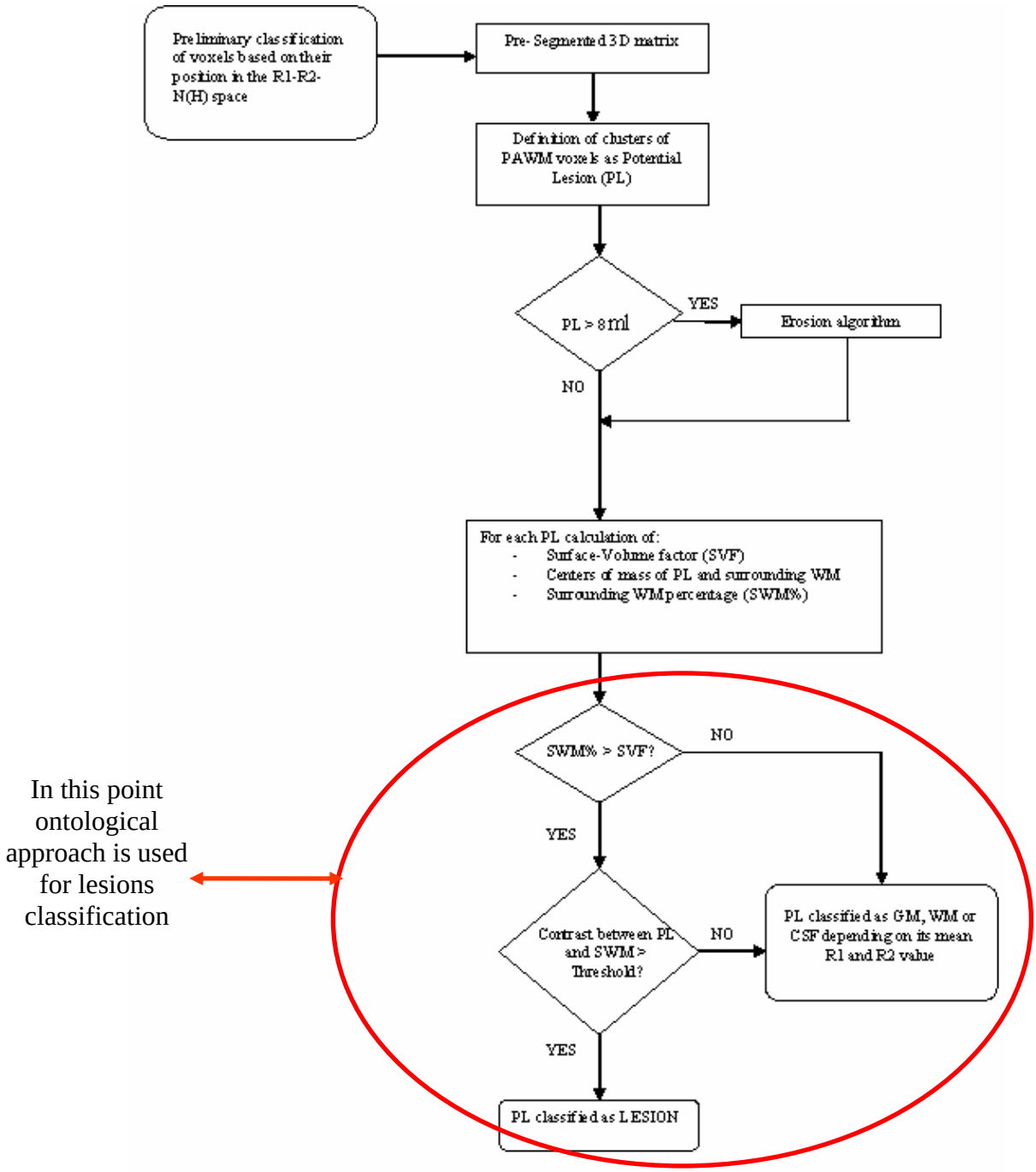

Figure 2 – Flow chart of the procedure for the classification of lesions

Since in the multifeature space the MS lesions partially overlap the normal tissue distribution , voxel position alone does not permit unequivocal classification of MS lesions, but only allows the definition of a ROI for tissues that can be classified as *PAWM* (*Potentially Abnormal White Matter*). The voxels of the different tissues are classified taking in account their position in the multifeature space by obtaining a presegmented 3D matrix. Then the 3D

clusters composed of PAWL voxels, are classified as normal tissue or as lesion. This process has three phases. The first step is the *identification of Potential Lesion* (PL) : the 3D matrix presegmented is scanned to find all PAWM voxels and to label them as PL. When a voxel of this kind is found, a 3D region growing is applied, using this voxel as a "seed" to define spatial cluster of spatially contiguous PAWM voxels. The second step is the *fragmentation of spatial cluster* in order to improve classification of large lesions, where there is a great probability of normal tissue voxels, included in the PAWM, connected to true lesions voxel. So large PLs probably include thin connection between normal and abnormal tissues. The last step is *the lesion classification*: spatial cluster are classified based on their shape, dimension and spatial relationship with white matter. A cluster is considered as lesion if it is small, roundish and surrounding by white matter, but , when the size of the lesion is larger , its shape can be more irregular and have an ample interface with grey matter. In order to classify cluster, for each Potential Lesion the following parameters are calculated:

- PL shape factor :

$$PLSF = \frac{n_b}{\sqrt[3]{n^2}}$$

  where n_b is the number of the voxels surrounding the PL and n is the number of voxels of the PL;

- PL dimension factor:

$$PLDF = \frac{1}{\sqrt[3]{n}}$$

- Surface-volume factor:

$$SVF = PLSF^{P1} \cdot PLDF^{P2}$$

  where P1 e P2 are factors determinated in the algorithm optimization;

- Center of mass of PL and of surrounding WM in the R_1, R_2, N(H) space according to the formula:

$$x_i = \frac{\sum_{j=1}^{n} x_{ij}}{n}$$

  where x_i is the i^{th} coordinate of the centre of mass of a tissue spatial cluster in the multifeature space and n is the voxels number of that cluster.

The most recent version of the algorithm includes all information that have been tested to verify if a PL is a plaque, in a single ratio, which is compared with a threshold experimentally obtained.
So a PL is classified as lesion if:

$$\frac{white\_p \cdot FFD}{dis\tan ce\_factor \cdot WMp} < threshold$$

where:

- *white_p* : percentage of white matter in comparison with all brain volume;
- *FFD* : shape dimension factor, it's the same of the factor SVF described before (the exponent P1 and P2 are usually equal to 1.1);
- *distance_factor* : distance between outline and lesion in the R2, PD plan;
- *WMp :* percentage of white matter surrounding lesion;
- *threshold* : it's numeric value compared with the ratio. In order to have right sensibility it has been experimented that a good value for the threshold is 0.82.

3 Construction of ontology and rules for the individuation of the lesions

If we want to replace the algorithmic approach for lesions classification with an ontological approach , the first step is building an ontology. So we have identified the relevant domain concepts that correspond with ontology classes. Then properties and rules have to be defined.

CLASSES

The following classes have been introduced into the ontology:

- BrainTissue
  - WM
  - GM
  - SF
  - PL

where WM : white matter
GM : grey matter
CSF : liquor
PL : probably lesion (recognized by algorithm)

PROPERTIES

Properties are used to describe features and attributes of the classes. In this ontology there are only datatype properties with class PL as domain:

Property	Domain	Range
has_WMp	PL	Float
has_FFD	PL	Float
has_distance_factor	PL	Float
IS_LESION	PL	Boolean

For each instance of PL class, the first three properties allow to introduce respectively:

- surrounding WM percentage;
- shape-dimension factor;
- distance factor;

Instead property IS_LESION is set *true* or *false* by rules application: it's *true* when PL is supposed to be a lesion, *false* in the opposite case.

In Appendix there is the ontology definition by OWL language.

RULES

We need some rules to recognize lesions, starting from the set of all probably lesions found by algorithm. A rule has an antecedent and a consequent:

antecedent → *consequent*

whenever the conditions specified in the antecedent hold, the conditions specified in the consequent must also hold.

From a study about lesions of Multiple Sclerosis, supported by interviews to experts, three essential features of a lesion have been found:

- a lesion must be surrounded by a high percentage of white matter ;
- a lesion has a roundish shape, at least when it is small, but when lesions number increases more lesions can join together and so they assume an oblong shape;
- a lesion has an high distance factor, which is the distance between lesion and outline in the R2, PD plane.

From this information, and from the analysis of MS lesions typical values of white matter percentage, surface-volume factor and distance factor, some rules have been deduced. When the instances of the class PL are introduced, all properties are set except IS_LESION. Rules allow to set this property.

1) *PL(PL1) ∧ has_WMp(PL1, WMP1) ∧ has_FFD(PL1, FFD1) ∧ has_distance_factor(PL1, DF1) ∧ greaterThan(WMP1, "0.601932") ∧ lessThan(FFD1,"2.227907") ∧ greaterThen(DF1, "0.93") → IS_LESION (PL1, "true")*

Rule 1 sets property IS_LESION as *true* if all the following conditions are verified at the same time: WM% > 0.601932, FFD<2.227907, DF > 0.93 . (Numerical values have been deduced from analysis of lesions recognized by algorithmic method, that we have used as reference point).

Rules 2, 3 and 4 set the property IS_LESION as *false* if one of that conditions about WM%, FFD and DF is not verified.

2) *PL(PL1) ∧ has_WMp(PL1, WMP1) ∧ lessThanOrEqual(WMP1, "0.601932") → IS_LESION (PL1, "false")*

3) *PL(PL1) ∧ has_FFD(PL1, FFD1) ∧ greaterThanOrEqual(FFD1, " 2.227907") → IS_LESION (PL1, "false")*

4) *PL(PL1) ∧ has_distance_factor(PL1, DF1) ∧ lessThanOrEqual(DF1, "0.93") → IS_LESION (PL1, "false")*

In Appendix there is rules definition by SWRL language.

4 Use of a reasoner for lesions classification

After ontology development we need a reasoner to apply rules to instances and to recognize the lesions.
The present reasoners, such as Racer, cannot be used for the application to the ontology and the rules for lesions classification, because they don't accept

datatype properties. So a reasoner developed at ICAR institute [3] has been used to obviate this problem: by using SweetRules tools, it translates DLP OWL ontology in SWRL rules, enables to use a single rules to process and reason in a correct and complete way and converts rules expressed in SWRL into owner Jena 2 syntax. So built-in functionalities for operations and numeric comparison and rule engine offered by Jena 2 can be used.

Some instances are introduced to test ontology and rules deployed for lesions classification, then the just described reasoner is started in order to apply rules to the instances. A query is used to ask which instances of PL classes have property IS_LESION as *true*.

5 Preliminary test for lesion recognition

Ontology and rules for lesions recognition has been tested on a real case belonging to an nationwide itinerant study.
In order to test all in automatic way, a simple Java program has been created, its input is a file containing information about the potential lesions, produced by algorithm, and the program return a text file only with information of found lesions.
The ontological approach enters the algorithm after identifying of the potential lesions and writing information file, which contains the data of the PLs: lesion number, coordinates of the lesion barycentre, coordinates of the surrounding white matter barycentre, distance factor, dimension factor, shape factor , dimension-shape factor, percentage of surrounding white matter, number of surrounding voxels, number of surrounding voxels of white matter, limits of the lesion, lesion seed , voxels number of the lesion.
The user is asked to indicate the file of lesions information. This file is read to obtain and to save identificative number, percentage of white matter, dimension-shape factor and distance factor. Each potential lesion is introduced as instance of PL class with all properties set as the values of the corresponding lesion.
After the suitable transformations of the language mentioned before, reasoner applies rules to the instances, so the property IS_LESION is set *true* or *false* according to the case. Then a query allows to identify all instances of class PL for which the property IS_LESION is set as *true.* In the end results are written in a text file to use them for a possible check on QMCI images.

A set of 4849 PLs has been produced by algorithm.

Algorithmic approach has found 23 lesions from this set, while ontological method has given a set of 37 lesions as result, they are all the same lesions founded by the first approach plus other 14 lesions , so this last method shows a greater sensibility.

Adobe Photoshop software has been used to visualize slices obtained by QMCI technique, in order to verify the reliability of our results.

Different tissues are shown in images with different colours. Besides three channels RGB, there is a channel to display all PLs, another one for lesions found by algorithm, a channel for lesions found by ontological approach and a last one to show lesions found by both the approaches.

For example , in figure 3 there is a slice for which the application of the two different methods brings to the same result, finding the same lesions.

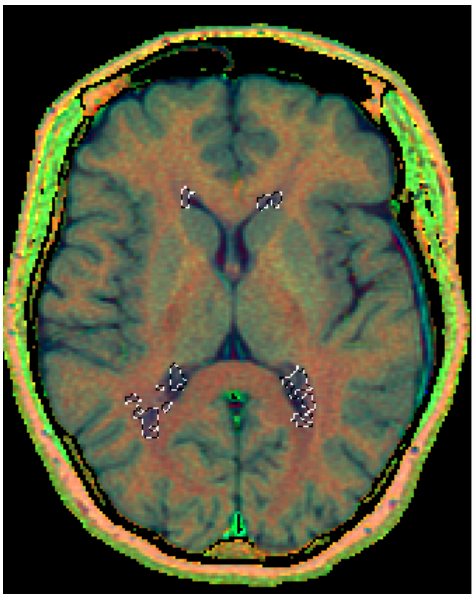

Figure 3 – Slice QT267

In figure 4 , four subsequent slices are showed; in these slices the ontological approach finds a lesion, that is not found by algorithmic approach. So method based on ontology and rules shows a grater sensibility.
From a visual analysis this is not a simple lesion , but a lesion connected to a sulcus slightly. Probably this is derived by an wrong plaque fragmentation, executed by algorithm in the step of PL individuation, so lesion area has been united with a sulcus.

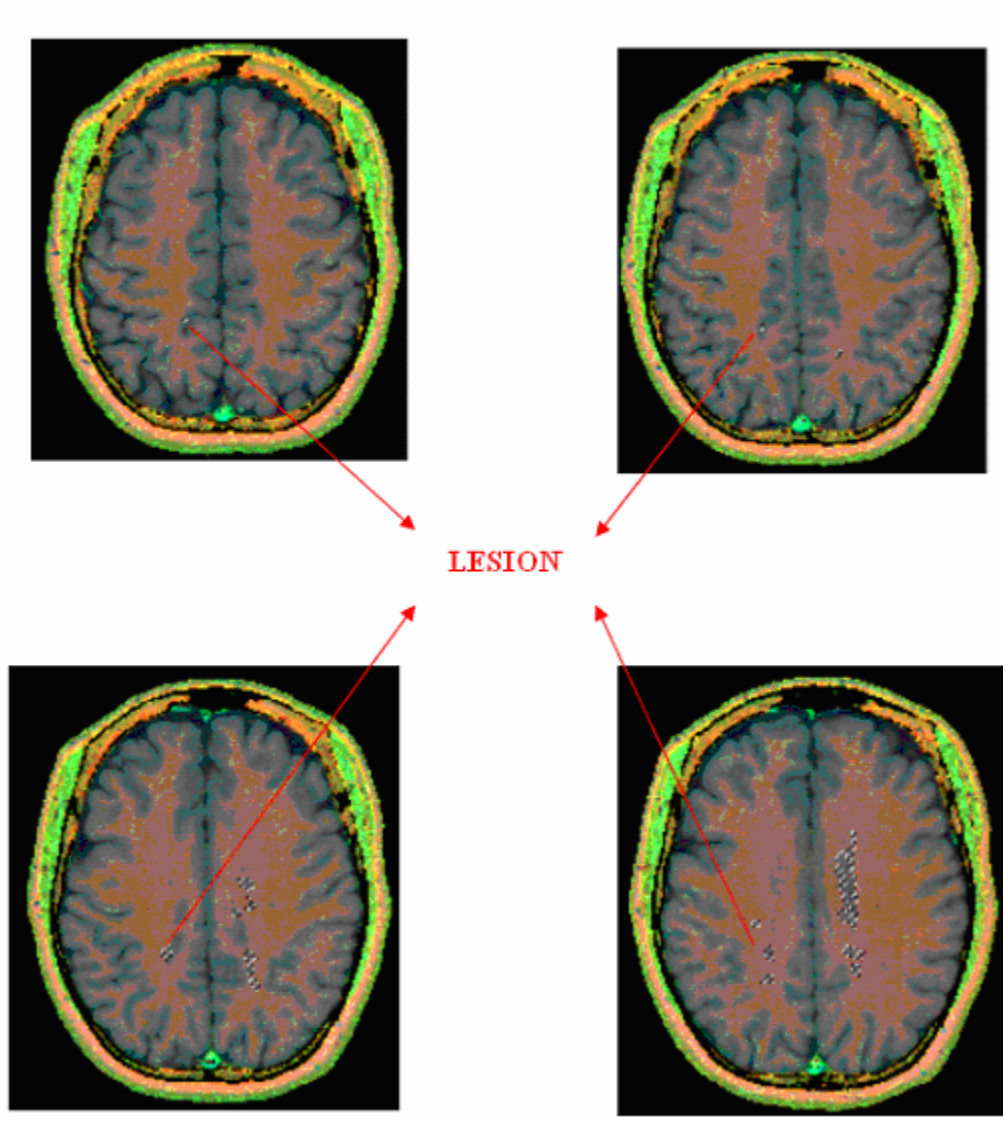

Figure 4 – Slices QT274, QT273, QT272, QT271

Beyond the number of founded lesions, which is determinated by greater sensibility of a method than the other, the important thing to be underlined is the fundamental difference of the used approach. With the ontology method, a metalanguage has been used, so we are in a higher semantic level then the other case in which an algorithm is used.
For example with the ontological approach, if we want to modify the sensibility of the method, changing thresholds in the file of SWRL rules is enough, without a recompilation, that is necessary with the algorithmic approach.

Lesions found by two approaches have been selected from slices and it has been established if they were or not lesions thanks to the help of an expert.

About the additional lesions :

- Most of them is referred to cerebellum area, but this is a critical zone, where usually there are not lesions; so this area has not been considered when we have made our examination in the images. (In order to consider this criticality, the ratio used to verify if a PL is or is not a lesion, has been modified, multiplying it by 1.4. So this ratio is hardly less then the threshold 0.82 and PL is not recognized as a lesion. There isn't this modification in the case of ontological approach) ;
- 5 are false-positive ;
- 2 are lesions, although a little piece of sulcus is caught together with them;
- for the remaining lesions there is doubt because it's difficult distinguish them into the slices.

Conclusion and perspectives

An ontology, integrated with right rules, can give a simple and effective alternative to an algorithmic method , when MS lesions have to be individuated. The method proposed in this paper could be improved , refining rules for the individuation of the plaques, for example considering the criticality of cerebellum area. Then the possibility of a classification of brain anatomical entities could improve the method of lesions classification noticeably: all elements incompatible with lesions cold be excluded a priori, so attention could be moved towards other places where plaques are more probably. For example, if we know that in a certain place there is a sulcus, then we know that it's impossible recognize as lesion the area which coincide with it or that is very near to it. Now, only anatomical information, useful to recognize lesions, concerns spatial position and symmetry, but these elements don't give guarantees because they can change very much according to the subject.

Acknowledgments

This work has been realized with the precious collaboration of PhD Bruno Alfano.

References

[1] “Automated Segmentation and Measurement of Global White Matter Lesion Volume in Patients with Multiple Sclerosis”, Journal of Magnetic Resonance Imaging 12:799-807 (2000) - Alfano B., Brunetti A., Larobina M., Quarantelli M., Tedeschi E., Ciarmiello A., Covelli E., Salvatore M.

[2] “Anatomia Umana”, vol. 3 , edi-ermes, 2000 - Balboni, Bastianini, Brizzi, Castorina, Comparini, Donato, Filogamo, Fusaroli, Lanza, Grossi, Manzoli, Marinozzi, Miani, Mitolo, Motta, Nesci, Orlandini, PAssaponti, Pizzini, Reale, Randa, Ridola, Ruggeri, Santoro, Tedda, Zaccheo

[3] “An ontology service for supporting reasoning in medical applications”, ICAR-CNR technical report, TR-06-09 (2006) – G. De Pietro, M. Esposito

[4] “Un approccio basato su ontologie per la descrizione anatomica del cervello e la classificazione di potenziali lesioni da sclerosi” – tesi di laurea , Università degli Studi di Napoli *Federico II* - Esposito A. – 2006

APPENDIX

Ontology definition by OWL language:

```
<?xml version="1.0"?>
<rdf:RDF
    xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
    xmlns:xsd="http://www.w3.org/2001/XMLSchema#"
    xmlns:rdfs="http://www.w3.org/2000/01/rdf-schema#"
    xmlns:owl="http://www.w3.org/2002/07/owl#"
    xmlns:dc="http://purl.org/dc/elements/1.1/"
    xmlns="http://www.medicalOntology/Lesioni.owl#"
    xml:base="http://www.medicalOntology/Lesioni.owl">


  <owl:Ontology rdf:about="">
  </owl:Ontology>

  <owl:Class rdf:ID="brainTissue"/>
  <owl:Class rdf:ID="GM">
       <rdfs:subClassOf rdf:resource="#brainTissue"/>
             <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
                    GREY MATTER
             </rdfs:comment>
  </owl:Class>
  <owl:Class rdf:about="#CSF">
             <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
                   LIQUOR
             </rdfs:comment>
       <rdfs:subClassOf rdf:resource="#brainTissue"/>
   </owl:Class>
   <owl:Class rdf:about="#WM">
       <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
             WHITE MATTER
       </rdfs:comment>
       <rdfs:subClassOf rdf:resource="#brainTissue"/>
   </owl:Class>
   <owl:Class rdf:ID="PL">
       <rdfs:subClassOf rdf:resource="#brainTissue"/>
       <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
             PROBABLY LESION
       </rdfs:comment>
   </owl:Class>

   <owl:DatatypeProperty rdf:ID="has_WMp">
       <rdfs:range
rdf:resource="http://www.w3.org/2001/XMLSchema#float"/>
       <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
       WMp=Percentage of white matter surrounding lesion
       </rdfs:comment>
       <rdfs:domain rdf:resource="#PL"/>
   </owl:DatatypeProperty>

   <owl:DatatypeProperty rdf:ID="IS_LESION">
       <rdfs:domain rdf:resource="#PL"/>
```

```
       <rdfs:range
rdf:resource="http://www.w3.org/2001/XMLSchema#boolean"/>
       <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
       It’s "true" when PL is classified as lesion
       </rdfs:comment>
   </owl:DatatypeProperty>

   <owl:DatatypeProperty rdf:ID="has_distance_factor">
       <rdfs:comment
rdf:datatype="http://www.w3.org/2001/XMLSchema#string">
             distance factor : it’s the distance between lesion and
its outline in the multifeature space (less then or equal 1)
       </rdfs:comment>
    <rdfs:domain rdf:resource="#PL"/>
    <rdfs:range
rdf:resource="http://www.w3.org/2001/XMLSchema#float"/>
   </owl:DatatypeProperty >

   <owl:DatatypeProperty rdf:ID="has_FFD">
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       Surface-volume factor
     </rdfs:comment>
     <rdfs:domain rdf:resource="#PL"/>
     <rdfs:range
rdf:resource="http://www.w3.org/2001/XMLSchema#float"/>
   </owl:DatatypeProperty>

</rdf:RDF>
```

Rules definition by SWRL language:

```
<?xml version="1.0" encoding="UTF-8"?>
<rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
          xmlns:swrl="http://www.w3.org/2003/11/swrl#"
          xmlns:owlx="http://www.w3.org/2003/05/owl-xml"
          xmlns:ruleml="http://www.w3.org/2003/11/ruleml"
          xmlns:swrlx="http://www.w3.org/2003/11/swrlx">

          <swrl:Variable rdf:about="#PL1"/>
          <swrl:Variable rdf:about="WMP1"/>
          <swrl:Variable rdf:about="FFD1"/>
          <swrl:Variable rdf:about="DF1"/>


       <swrl:Imp>
             <swrl:head rdf:parseType="Collection">
                   <swrl:DatavaluedPropertyAtom>
                         <swrl:propertyPredicate
rdf:resource="http://www.medicalOntology/Lesioni.owl#IS_LESION"/>
                                  <swrl:argument1>
                                        <swrl:Variable
rdf:about="#PL1"/>
                                  </swrl:argument1>
                                  <swrl:argument2
rdf:datatype="http://www.w3.org/2001/XMLSchema#boolean">false</swrl:ar
gument2>
```

```
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            <swrl:body rdf:parseType="Collection">
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                              <swrl:argument1>
                                    <swrl:Variable
rdf:about="#PL1"/>
                              </swrl:argument1>
                              <swrl:argument2>
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                              </swrl:argument2>
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st>
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                              </rdf:rest>
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                              </swrl:argument1>
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                              </swrl:argument1>
                              <swrl:argument2>
                                    <swrl:Variable
rdf:about="#FFD1"/>
                              </swrl:argument2>
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or"/>
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rdf:about="#PL1"/>
                              </swrl:argument1>
                              <swrl:argument2>
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rdf:about="#DF1"/>
                              </swrl:argument2>
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                              <rdf:first>
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                                          </rdf:first>
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```

```
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