Future implementation of automated analysis tools for Multiple Sclerosis on conventional magnetic resonance imaging.

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*, + Equal contribution
ABSTRACT

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Background: Magnetic resonance imaging (MRI) is imperative for the detection and characterization of Multiple Sclerosis (MS) lesions in the central nervous system. The revised McDonald's criteria of 2017 involve brain and spinal cord MRI lesions with respect to dissemination in time and space to aid in establishing the diagnosis. Furthermore, MRI is the principal tool of tracking brain and spinal cord changes and monitoring treatment effects and disease progression. Manual evaluation of multiple evolving MS lesions and particularly estimation of brain atrophy is difficult due to the time-consuming nature of longitudinal assessment, the complexity of brain volume estimation, and is subject to significant interobserver variability.

Objectives: This study aims to survey current commercial and freeware automated tools for lesion identification and brain volume monitoring. We evaluate the feasibility and identify barriers in the adoption of computerized tools in the clinical setting.

Methods: A literature search was performed in PubMed, and Google Scholar databases and publications on automated image evaluation tools in multiple sclerosis were identified and reviewed. Findings in other neurologic populations supplemented limited evidence on reliability and validity.

Results and conclusion: We evaluated various existing automated software packages suitable and specifically developed for the multiple sclerosis population, including SepINRIA, Icobrain, DeepMedic, and others. We confirmed the benefits of image analysis automation. We describe differences between available software models, their advantages and disadvantages. Notably, we identify challenges faced by existing software implementations representing an obstacle to their wide adoption, such as hardware requirements, price of purchase and maintenance, absence of a gold standard, and uncertainty of healthcare benefits. After exploring the barriers, we propose solutions to integrating automated image analysis into routine practice through the development of a quality assurance and decision support system.
Disclosure

Authors do not have any disclosures to state.
MRI as a diagnostic tool and follow-up tool

McDonald Criteria (2017) is the gold standard for CLINICAL diagnosis with integrated MAGNIMS 2016 modifications, now involves MRI as a significant tool concomitantly to clinical attacks.

- Dissemination of time and space are considered one of criterion to diagnose
  - **Time:** uses T1 + Gd enhancing lesion / no-enhancing lesion OR new T2 hyperintense lesion, or CSF-specific OCB
  - **Space:** T2 hyperintense lesion in 2 or more CNS areas
    - Periventricular, cortical/juxtacortical, infratentorial, Spinal Cord

MRI as paraclinical outcome measure; also part of No Evidence of Disease Activity (NEDA-3 and 4) for treatment monitoring

No Evidence of Disease Activity (NEDA)

Clinical Picture

- No clinical Relapse
- No EDSS Progression

Imaging

- T1 + gadolinium enhanced lesion
- T2 lesion
- Whole brain volume

NEDA-3

NEDA-4
Methods of image analysis in application to Multiple Sclerosis

Global brain volume changes: Myelin water fraction [1], atrophy [3]

T1 with Gadolinium or chronic T1 hypointense lesion > 6 months; referred to as “black holes” [2-3]

T2 hyperintense lesions

Diffuse Tensor Imaging [2]


Various imaging modalities

[1] Myelin water fraction
[3] T2 FLAIR lesions in MS patients

*[2] and [3] are in the same MS patient.

Existing commercial and other products used for MS image analysis

Various research has been done to automatically detect MS. Tools are currently available

- **SepINRIA**: Free software for brain MRI analysis
- **Icobrain**: Brain imaging AI
  - Stanford University Medical Center, USA
  - Dr. Magnet Kramare, Pro Diagnostic Group, Slovakia
  - Picture This by Jankharia Imaging Center, India
- **DeepMedic, MD-GRU, SIENA, MSMetrix**
## Comparison of automated tools

<table>
<thead>
<tr>
<th>Tool / Metrics</th>
<th>UI</th>
<th>Support</th>
<th>Accuracy (DICE)</th>
<th>Brain Part</th>
<th>Dataset</th>
<th>License</th>
<th>Popularity (Google Scholar + PubMed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SepINRIA</td>
<td>user-friendly</td>
<td>not available</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>free</td>
<td>82</td>
</tr>
<tr>
<td>SIENA-X</td>
<td>command-line based</td>
<td>available</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>free</td>
<td>261</td>
</tr>
<tr>
<td>Icobrain</td>
<td>user-friendly</td>
<td>available</td>
<td>0.87</td>
<td>hippocampi</td>
<td>MICCAI 2012 challenge</td>
<td>paid</td>
<td>50</td>
</tr>
<tr>
<td>MD-GRU</td>
<td>command-line based</td>
<td>available</td>
<td>0.94</td>
<td>brain stem</td>
<td>custom (n=20)</td>
<td>free</td>
<td>61</td>
</tr>
<tr>
<td>DeepMedic</td>
<td>command-line based</td>
<td>available</td>
<td>0.90</td>
<td>brain tumor</td>
<td>BRATS 2015 training database</td>
<td>free</td>
<td>583</td>
</tr>
<tr>
<td>SPM</td>
<td>user-friendly</td>
<td>available</td>
<td>0.92</td>
<td>white matter</td>
<td>Brainweb simulated MR images</td>
<td>free</td>
<td>500,000+</td>
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<tr>
<td>FreeSurfer</td>
<td>user-friendly</td>
<td>available</td>
<td>0.83</td>
<td>hippocampi</td>
<td>MICCAI 2012 challenge</td>
<td>free</td>
<td>26,997</td>
</tr>
</tbody>
</table>
Barriers for a wide acceptance of machine assisted tools for image analysis in clinical practice

- **Price**
  - Price of the analysis tool
  - Cost of implementing tool into clinical practice; reworking current system

- **Gold standard**
  - Number of automation tools available is overwhelming

- **Systems**
  - Hesitancy of healthcare systems to accept new tool into clinical practice
  - Requires ethics approval and intensive testing.
The road forward

- A tool for quality control, not a tool for clinical diagnosis; quality assurance tool for MS cases as same way with lung and breast carcinoma
- There are purely logistical barriers to implement these tools. Future studies can focus to validate these tools in comparison to radiologist’s accuracy
- Development of integrative tools to compare images overtime can be beneficial and act as a support to diagnosis and surveillance. This would further carry less medicolegal risk.
- There was a MS lesion segmentation tools challenges that are developed to create and modify the current tools. Therefore, there will likely be further automated tool development in the near future.
