Published in final edited form as:

Comput Med Imaging Graph. 2015 December ; 46(Pt 2): 257–268. doi:10.1016/j.compmedimag.2015.09.007.

Design and development of an ethnically-diverse imaging informatics-based eFolder system for multiple sclerosis patients

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Abstract

Purpose—MRI has been used to identify multiple sclerosis (MS) lesions in brain and spinal cord visually. Integrating patient information into an electronic patient record system has become key for modern patient care in medicine in recent years. Clinically, it is also necessary to track patients' progress in longitudinal studies, in order to provide comprehensive understanding of disease progression and response to treatment. As the amount of required data increases, there exists a need for an efficient systematic solution to store and analyze MS patient data, disease profiles, and disease tracking for both clinical and research purposes.

Method—An imaging informatics based system, called MS eFolder, has been developed as an integrated patient record system for data storage and analysis of MS patients. The eFolder system, with a DICOM-based database, includes a module for lesion contouring by radiologists, a MS lesion quantification tool to quantify MS lesion volume in 3D, brain parenchyma fraction analysis, and provide quantitative analysis and tracking of volume changes in longitudinal studies. Patient data, including MR images, have been collected retrospectively at University of Southern California Medical Center (USC) and Los Angeles County Hospital (LAC). The MS eFolder utilizes web-based components, such as browser-based graphical user interface (GUI) and web-based database. The eFolder database stores patient clinical data (demographics, MS disease history, family history, etc.), MR imaging-related data found in DICOM headers, and lesion quantification results. Lesion quantification results are derived from radiologists' contours on brain MRI studies and quantified into 3-dimensional volumes and locations. Quantified results of white matter lesions are integrated into a structured report based on DICOM-SR protocol and templates. The user interface displays patient clinical information, original MR images, and viewing structured reports of quantified results. The GUI also includes a data mining tool to handle unique search queries for MS. System workflow and dataflow steps has been designed based on the IHE post-processing workflow profile, including workflow process tracking, MS lesion contouring and

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quantification of MR images at a post-processing workstation, and storage of quantitative results as DICOM-SR in DICOM-based storage system. The web-based GUI is designed to display zero-footprint DICOM web-accessible data objects (WADO) and the SR objects.

Summary—The MS eFolder system has been designed and developed as an integrated data storage and mining solution in both clinical and research environments, while providing unique features, such as quantitative lesion analysis and disease tracking over a longitudinal study. A comprehensive image and clinical data integrated database provided by MS eFolder provides a platform for treatment assessment, outcomes analysis and decision-support. The proposed system serves as a platform for future quantitative analysis derived automatically from CAD algorithms that can also be integrated within the system for individual disease tracking and future MS-related research. Ultimately the eFolder provides a decision-support infrastructure that can eventually be used as add-on value to the overall electronic medical record.

1. Introduction

1.1. Multiple Sclerosis and MRI

Multiple Sclerosis (MS) is a demyelinating disease in which the patient's central nervous system (CNS) degenerates and causes inflammation and brain and spinal atrophy [1,2]. The scarred tissues leftover from the autoimmune attacks are lesions, or plaques, in the white matter [3]. As the disease progresses, the effect on a patient's life can be devastating. Disability can continue to progress until an effective treatment regimen is developed for an individual patient to slow disease progression. Direct medical costs and associated assistive and rehabilitative expenditures can quickly reach into tens of thousands of dollars per year.

There is currently no cure for MS because of the irreversible axonal injuries and the complex nature as to what triggers the autoimmune attacks [3,4]. MS manifests itself differently amongst different ethnicities [5,6], such as differing prevalent symptoms, disabilities, MS lesion locations, and response to treatments. The purpose of an MRI scan is to visually locate lesions in the central nervous system. MS lesions appear hypo- or iso-intense in a T1-weighted scan and hyper-intense in a T2-weighted and FLAIR (fluid attenuated inverse recovery) scans. Location and morphology of lesions are also used to identify lesions caused by multiple sclerosis [7,8]. Fig. 1 shows the three aforementioned axial slices of a patient's brain with multiple sclerosis.

MS disease progression can be monitored by subsequent MR scans for changes in lesion characteristics in longitudinal studies. In general, following initial diagnosis, disease activity is assessed by the number of relapses per year (relapse rate), accumulation of disability as measured by the expanded disability status scale (EDSS) [9] and changes in MRI lesion characteristics. The progression of the disease is variable, and requires routine follow-up imaging studies to document disease exacerbation, improvement, or stability of the characteristic MS lesions.

1.2. Current challenges with MS disease management and research

There are a few challenges that exist in the current status for the diagnosis and treatment of multiple sclerosis in both clinical and research settings. MS is a complicated disease that

manifests itself differently for different individuals as well as different ethnicities. Therefore, MS disease management and treatment become complex and highly individualized. A more detailed study of specific clinical markers at the time of presentation and during the disease course is required to ascertain and define the distinct features of MS.

Currently, MS lesion quantification requires a manual approach to lesion measurement on MRI [9]. It is time-consuming to quantify lesion load (total lesion volume in a study), and volumetric calculations with current techniques only yielding, at most, a rough estimate. The task of tracking MS lesion changes becomes even more difficult if several MR longitudinal studies of the same patient (follow-up studies) require quantitative comparison, which is currently not utilized in clinical diagnosis. In addition, it has been shown that MS diagnosis, lesion detection and lesion load calculation suffer from inter- and intra-observer variability [10].

1.3. MS eFolder design concept

In order to build a complete system to aid in multiple sclerosis diagnosis, treatment, and research, we have designed and developed an ethnically-diverse imaging informatics-based system, called MS eFolder, designed specifically for MS clinical care and research. The MS eFolder provides a database solution for storing patients' clinical information, an effective way for accessing patients' MR images and associated data, and also provides a lesion quantification tool. By integrating these components compliant to the DICOM standard in the clinical environment, the eFolder system is able to provide a data repository for treatment planning, correlate MR lesion quantification data with clinical manifestations more effectively, and provide a data mining tool for research purposes. In the future this system can serve as the decision-support component in an overall EMR for treatment of MS patients. The concept of eFolder is derived from electronic patient records (ePR). ePR is a digital, comprehensive patient database that stores patients' demographic information, medical history, and any information that may be needed and included in ePR's designs. For example, an ePR developed for surgery [11] may contain a subset of patients that have a particular back pain related disease, for example, patients undergoing spinal discectomy.

The MS eFolder is developed to aid in diagnosis, disease tracking, treatment, and research of MS. After examining the needs of clinicians and for research purposes, the system has three main software components:

1. A DICOM-based patient record database: The database needs to store the patients' various information, such as their demographic information, medical history, MS history, and any survey results that are gathered by researchers and clinicians. The system also needs to link to medical images (in this case, patients' brain and spinal MRI) to aid in diagnosis and disease tracking. MR images and DICOM-SR objects are stored in the eFolder's image repository component, which will be explained in detail in the next section.
2. Image processing module: In order to quantify 3-dimensional white matter lesion volumes and brain matter volumes, an image processing module is included in the MS eFolder system. The module allows users to manually identify and contour lesions in the brain MRI. Another algorithm is able to

segment gray matter, white matter, and cerebro-spinal fluid (CSF). A voxel-based algorithm is able to cluster those contours and segmentations and quantify volumetric data. Its advantages include a standardized quantification process, allowing MS lesion tracking in longitudinal studies, and offering a quantifiable results for clinical trials and research. The module is integrated with the database, thus the results are stored and patient data can be queried via lesion characteristics. While the module currently utilizes manual contours to create MS lesion segmentation for volumetric calculations, we can replace the manual contouring component with an automatic or semi-automatic computer-aided detection (CAD) algorithm. The eFolder system's modular design allow the components to be replaced with minimal disruption of system services.

3. A web-based graphical user interface (GUI): A GUI is needed for patient data viewing, input, management, and data querying. It is web-based such that the system can be accessed via Hypertext Transfer Protocol (HTTP) and Internet connections. The GUI needs to be comprehensive such that all patient data, including diagnostic MR images and quantification results, are all available for viewing. The interface has the potential to be a powerful tool in data mining for researchers and data gathering for both clinical and research purposes.

The last step of MS eFolder system design is to integrate all of the components of eFolder together and fit into a real-life clinical workflow. IHE (Integrating the Healthcare Enterprise) provides a design of how to include a post-processing step inside a typical clinical workflow [12]. The MS eFolder system workflow is modeled after this IHE workflow profile to ensure successful DICOM-based integration when the system is available for clinical use.

2. Material and methods

Fig. 2 shows the components diagram of the MS eFolder system. The eFolder system consists of three components: eFolder web-based services, the image processing and quantification module, and a graphical user interface.

The system diagram also includes DICOM services (shown in Fig. 3 as orange block on the left) for receiving and storing MR images and DICOM SR objects, and also directing image workflow within the eFolder system. Patient data and images are stored in the eFolder archive server. The DICOM receiver acts as the gateway between image source and image archive. The control device directs image dataflow within the eFolder server, and the data archive acts as image repository in the system. The following sections detail design and development of these components.

2.1. EPR design

The eFolder database, written in MySQL, stores text data including patient history, MR image locations, and lesion quantification results. The database structure is built such that one single patient has a unique data entry regarding demographics and social data, has a list of all MR studies regarding to MS, and a list of all quantification results (in SR format) available for that patient. Fig. 3 shows the general database structure.

The information stored in demographic data includes name, gender, ethnicity, birthplace, and social history. The medical history database module stores records of any childhood illnesses, vaccines, and other past medical histories. The MS history database includes the year of first diagnosis/symptom, any family members with MS, MS type, MS symptoms and frequency, treatment history, and so forth. Data collection is conducted by patient interviews reading of medical reports, and physician inputs. Columned items are collected from surveys designed by neurologists and research project leaders.

The imaging database stores patients' MR studies. The database structure is designed following the DICOM standard, from the patient level to the study level, series, and finally individual images. Data in the imaging database is automatically populated via PHP-based DICOM parsing scripts. Table values, such as study instance UID (unique identification) and series instance UID are parsed directly from the header files of the uploaded DICOM images. DICOM patient identifiers are matched with patient records in the demographics database during the uploading procedure via web-based GUI.

The lesion quantification algorithm produces results from both the study level and at image level. At the study level there are total lesion load, number of lesions, three-dimensional lesion centroid coordinates, lesion sizes in three-dimensions, and the overall report of findings and three-dimensional view of the lesion contours. At the image level, the program calculates lesion locations on that image, size of each lesion on the image, and (x,y) coordinates of lesion contours. Lesion volume data calculation and population of database is covered in the next sections.

2.2. Lesion detection and quantification

The eFolder system is designed to include a post-processing module that detects MS lesions and calculates lesion volumes in the white matter region of central nervous system. The purpose of the module is to objectively quantify lesion volumes and able to track lesion volume changes in longitudinal studies. The quantified changes enables users to track disease progress and monitor treatment responses over time. The module receives raw DICOM data from the modality or any other image data source and automatically detects abnormal voxels as MS lesions. Then, the lesion quantification algorithm is designed to output lesion volumes, lesion locations, and total lesion load from lesion contours on the brain MRI.

While the lesion detection component is being concurrently explored and developed, we have designed the system based on the assumption that the detection and quantification component has been completed and able to generate reliable results. Therefore, the system is modular, and the detection component can be replaced by any new or existing MS lesion detection algorithms. In recent years, there have been several interests and attempts at MS lesion detection with various degrees of success [13–15]. Any existing or future MS lesion detection and segmentation can be implemented in the MS eFolder system because of the modular design.

With this in mind, we currently use lesion contours manually completed by radiologists and evaluated by neuroradiologist fellows in order to achieve better accuracy and detection and

contouring, as well as completing overall system development. The MRI studies are uploaded to Synapse3D[®] software at Healthcare Consultation Center II (HCCII) at the University of Southern California. With the software, users are able to manually draw lesion contours directly on the DICOM images. The contours are exported via DICOM files. The output of lesion identification is then evaluated by the quantification algorithm.

Lesion voxels in the binary segmentation are clustered in 3-D with 26-connectivity principle. The lesion load (total lesion volume in the brain) and the number of lesions can be calculated using these clusters. Lesion volume is obtained by multiplying number of voxels in a lesion and the voxel size, which is extracted from DICOM headers of images. Lesions are separated into three subgroups: small ($<1 \text{ cm}^3$), medium (between 1 and 5 cm^3), and large ($>5 \text{ cm}^3$). Lesion load is obtained by summing up all lesion volumes, and lesion locations are identified by the coordinates of their centroids.

2.3. Quantification results output and reporting

The initial output of the lesion quantification program is a MAT-LAB file containing total lesion load, lesion coordinates, volume of each lesion, number of lesions, 2D MR slices containing lesion contours and lesion reconstructed in 3-D space. The algorithm produces output data that needs to be standardized and integrated with other system components for data queries and look-ups. DICOM structured reporting (DICOM-SR) provides templates to include quantification results in a standardized format [16]. The structured reporting would allow searching, storage, and comparison with other similar data better than traditional paper report format.

For integrating the image processing module in the overall system, we are using the methodology outlined in a CAD-PACS integration toolkit. A CAD-PACS integration toolkit is used to store CAD results in a Picture Archiving and Communications System (PACS) environment [14]. While the eFolder system currently does not use CAD programs and CAD results to identify MS lesions, the output of lesion quantification algorithm is considered as post-processed results similar to CAD outputs and can be stored via a DICOM-SR. An integration of quantification results with DICOM-SR is designed and implemented to directly store quantification results in a tabulated format in the eFolder, as well as to produce DICOM structured reports that may be displayed from a PACS workstation and stored in a conventional PACS. The utilization of DICOM-SR and CAD-PACS toolkit for MS eFolder is for a more streamlined workflow in a standardized way that can be implemented in existing PACS environments. Fig. 4 is a template designed for storing lesion quantification results.

After designing the custom template for lesion quantification results, Fig. 5 shows the workflow steps of converting MATLAB-based quantification results into DICOM-SR objects.

The first step is to convert quantitative results to an XML (Extensible Markup Language) document, which then is converted to DICOM-SR via the dcmtool open-source toolkit [18]. In order to generate the correct XML document, sample DICOM SR files obtained and converted to XML. The XML template then is modified and customized to store the

quantification values. A MATLAB script is used to convert quantitative output from a study to the XML file according to the customized template. Fig. 6 shows a partial screenshot of the resultant XML document.

2.4. Visualization

The following are the design criteria for the eFolder user interface:

- The GUI needs to be web-based to allow remote access using thin-client architecture. Computations and visualizations are completed on the server side for a light-weight and fast GUI.
- The GUI needs to be comprehensive. It needs to display patient clinical data, imaging data, and quantification results on the same interface. It allows physicians and radiologists to access all of the information related to the data query.
- The system needs to be dynamic and allow display of 3D images and manipulations of images presented. An organized viewing interface allows for a more clarified presentation
- The GUI needs to allow flexible and intelligent data mining. With a large number of patients' information stored in the eFolder system, any clinician and researcher should be able to look up MS patients on a variety of different search criteria, ranging from patient demographic data to lesion analytical results.

Base on PHP scripting language, the dynamic GUI guides the user to look up a specific patient's disease history with images, and it allows querying for patients with various different criteria. Viewing of DICOM images allows zoom, pan, window/level, and scrolling on the webpage. Fig. 7 shows a screenshot of the comprehensive web-based GUI for MS eFolder.

The developed GUI fits all of the design criteria described above. The GUI is web-based and hosted on a secure HTTP server. Users are able to log in using his or her credentials to view patient data. The main page of the GUI displays all of the essential patient information, such as name, ID, date of birth, gender, and ethnicity. The GUI is then divided up into different tabs, both within the main GUI as well as separated browser tabs. The main window module of patient information (on the left panel of Fig. 7) contains “MS History”, “Medical History”, and “Social History”. User may click on each tab to switch between viewing the three data sets. The top right module contains the WADO-based image viewer embedded within the main window. The user may view the imaging studies separately in a full-size DICOM image viewer tab. The right bottom panel displays the DICOM-SR result from the patient's study in a tabulated format. The main window's purpose is to aggregate all of the information and display it in a clear and organized way.

The GUI also allows patient data input and patient data look-up via web-based forms. The data lookup feature is able to allow user to access all of the patients within the query criteria in the form. The criteria include patient clinical data as well as imaging and lesion

quantification data. This feature is designed to allow data mining of eFolder patient database, allowing user to access a large data source to obtain data. The resultant data analysis may create observable trends that were previously difficult to obtain. For example, user may look up patients that have had certain drug treatment for over 5 years, while simultaneously looking up if the patients has had imaging scans during that time. The changes in lesion volumes and locations may shed a light on treatment's effects on the imaging level over time.

In addition, the system GUI is designed for user to view quantification results visually via the WADO viewer. DICOM secondary capture, or DICOM-SC, are DICOM image objects generated by postprocessing clients and software packages. In the eFolder project, DICOM SC are image captures of lesion contour results. DICOM-SC, along with SR, aids users to visualize MS lesion contours in both 2D and 3D space. The secondary captures of contour results are converted to the DICOM format for storage and display from a DICOM image viewer, for streamlining the DICOM-compliant workflow in the MS eFolder system. For 2D image captures, a MATLAB script is used to overlay 2D lesion contours on top of the FLAIR axial images to create a new series under the DICOM study. DICOM-SCs are stored in the archive and can be viewed alongside the original DICOM images in the DICOM web-based viewer. Fig. 8 shows how the DICOM images and SCs are viewed in a WADO (web accessible DICOM objects) viewer.

2.5. Integration

The MS eFolder design is modeled after the IHE workflow profile to show its use in a clinical environment. To accomplish the tasks, a simulated clinical environment with MS eFolder is set up in the Image Processing and Informatics laboratory (Fig. 9).

The workflow for MS eFolder integration is defined in five steps:

1. MR images are sent from modality simulator to the eFolder server for archiving
2. The eFolder server sends a copy of the images to the postprocessing workstation for postprocessing analysis
3. User at the contouring workstation is able to access the images via contouring software
4. Lesion contour files are analyzed by the volume quantification module, which converts quantification results into DICOM_SR and sent back to the eFolder server for storage
5. At the completion of each of the previous steps, a status tracking tool inside eFolder displays alerts of the study progress to the user

Fig. 10 displays the physical components diagram of the MS eFolder system setup in order to simulate the workflow steps outlined in Fig. 11.

The hardware environment is set up in a laboratory environment. There are two Windows-based desktop towers, one performs as the eFolder archiving and web server and the other as

the post-processing workstation. Another laptop is connected to the network to simulate the user accessing the eFolder system. The eFolder network is LAN-based, connected via Ethernet cables and managed by a router. The router, a D-Link EBR 2310 series wired router, assigns unique IP addresses to the hardware components in the network. The eFolder web/archiving server is a Dell® Dimension 9150 series desktop tower, running Windows XP Professional. A WAMP (Windows Apache/MySQL/PHP) server program is installed on the desktop to run the eFolder's web-based interface, PHP scripts such as database connection and DICOM parsing, and the MySQL-based eFolder database. The post-processing workstation is a Dell® Dimension 9200 series desktop tower, running Windows 7 Professional. MATLAB version 2011b is installed on the post-processing workstation to run the volume quantification module. The post-processing workstation also includes web-based Synapse3D interface for lesion contouring. The laptop is used to access the system, and there are no system requirements as long as the laptop has a web browser to view the eFolder GUI. This allows the eFolder system to be accessed on the network by portable devices such as tablet computers or smart mobile phones. Fig. 11 shows a status tracking module of the MS eFolder interface that tracks a study's progress in the eFolder study acquisition workflow.

3. Results and discussion

3.1. Data collection

The MS eFolder system requires patient clinical data and MR imaging data for designing and building the infrastructure in this phase. In order to build and validate the system, sample patient data are acquired from the Department of Neurology and Department of Radiology at University of Southern California (USC). There are two main goals of data collection: the first goal is to acquire sample data to build the system infrastructure, and the second goal is to acquire an adequate number of data to complete system validation and evaluation.

Research regarding differences in Hispanic American MS patients is the primary motivation for data collection among the different ethnic groups. Compared to the detailed MS studies regarding African American and Asian ethnic groups, there has not been these kind of studies performed related to Hispanic MS patients. A research project on Hispanic-American MS patients has been ongoing at USC to observe any significant differences in disease manifestation or correlations between Hispanic and Caucasian MS patients. The MS eFolder is thus currently designed to fit the data model of Hispanic American-related research data.

For each MS patient, two types of data are collected: clinical data and imaging data. Patients' clinical data are collected via physicians' questionnaires about their social and medical backgrounds. Patient candidates' criteria include having been diagnosed of multiple sclerosis, having had appointments at the Neurology department at USC, and having had MR brain images (T1-w, T2-w, and FLAIR axial slices) taken at various imaging centers and available in digital format at USC. Patient data collection has begun at USC since 2008. Patients visiting the MS clinic were asked to fill out a questionnaire form regarding their

basic information, social history, ethnic background, medical history, and childhood medical history. A sample form is shown in Fig. 12.

All brain MR studies are collected at University of Southern California Academic Medical Center and Los Angeles County Hospital. A total of 72 patients are collected: 36 Hispanic and 36 Caucasian patients. The patients of two groups are matched by gender, age (within 5 years), disease duration (within 5 years), and disease type (all are relapse-remitting). For each patient, the images, in DICOM format and anonymized, are acquired from Siemens® Symphony Maestro 1.5T and GE® Signa HDt 1.5T MR scanners and include at least T1, T2, and FLAIR axial images as well as sagittal/coronal views, diffusion images, etc.

3.2. Lesion quantification and data analysis results

Fig. 15 shows the manual contour results from Caucasian and Hispanic patients, comparing total lesion volume and disease duration.

Fig. 13 is also an example of data mining tool of MS eFolder, shown in Fig. 2 as part of the GUI. The system is able to relate disease duration, obtained from patients' medical history, and lesion volume, which is obtained from MS eFolder's image processing module. The comprehensive data collection, storage, and analysis highlights the eFolder's capability of integrating patient data into a complete patient profile.

A longitudinal study tracking viewer module has been developed to help users track a patient's disease progress visually. Fig. 14 shows an example of data tracking of 4 longitudinal studies, and Fig. 15 shows comparison of lesion contours from two studies of the same patient. The two figures have both been included in the web-based GUI as separate viewing modules.

The GUI is able to display the lesion contour results in its quantitative analysis module, which can be viewed in a separate browser. The quantitative results, longitudinal analysis results, and lesion comparison results between the initial patient groups are all presented in the analysis module

3.3. Preliminary system development results

Preliminary tests of the MS eFolder system with integrated IHE workflow were successful in the laboratory environment. All 72 patients' information have been entered into the MS eFolder database, and the MR studies have been uploaded into the system for data transfer and data upload based on the DICOM protocol. Radiologists have completed manual contouring on all 72 patients plus any additional studies being collected. The output of manual contouring steps have successfully been quantified by the quantification module, and DICOM-SR objects of quantification results have been generated and stored. The comprehensive eFolder GUI and database has been successfully completed and is available for viewing via a web browser. The DICOM-SR conversion workflow has been completed and successfully tested within the system. Overall, the comprehensive GUI design and layout to display lesion quantification data in DICOM-SR has been completed.

The eFolder system will be implemented in a clinical environment as part of the future work. The system will be evaluated based on system performance, data uploading and viewing time, as well as patient data look-ups and data mining modules. The system will be able to display a patient's profile, with treatment history and disease changes over time, which includes quantified lesion changes. Users will also be able to look up lesion data and clinical data for a large group of patients in order to observe and discover any disease trends. The eFolder system, combined with very large amount of data generated in the clinical environment, is capable of performing complex big data analysis.

3.4. Future work

A major goal for our current development is to develop a reliable and accurate lesion detection algorithm in order to decrease manual contouring man-hours.

Our current progress on developing an automatic lesion voxel classification algorithm is based on Statistical Parametric Mapping (SPM) brain image analysis toolkit for MATLAB [19]. At first, gray matter and white matter of the brain are segmented via voxel intensity estimation and probabilistic maps provided from SPM, which utilizes voxel-based morphometry [20], or VBM. VBM of brain MRI involves spatially normalizing all of the images in a study into a standardized stereotactic space. The algorithm then extracts the gray and white matter voxels from normalized space, performs smoothing, and then performs a Bayesian statistical analysis to further calculate gray and white matter voxel probabilities [21]. The output of this SPM-based preprocessing is a probabilistic map of gray matter and white matter segmentation. After gray matter, white matter, and CSF have been segmented, we can calculate brain parenchymal fraction, as well as starting on segmenting MS lesions in white matter.

Once the automatic detection component is completed, the module will be integrated into the overall eFolder system by replacing the manual contouring component. The eFolder system has been designed in such a way that DICOM-compliant modules can be inserted into the system without significant changes in the overall system workflow. The automatic lesion detection will enhance the overall eFolder system, making it more efficient and consistent in quantifying lesion volume changes and achieving overall system goals. Since the eFolder system is designed with IHE integration protocols, any new or existing lesion segmentation programs can be integrated into the eFolder system with DICOM-compliant outputs and protocols.

There are a few other areas of the eFolder system that need further work and is currently under development. First, 3-dimensional DICOM-SC objects is being developed to be displayed in WADO viewer. Currently, a 3-D contour object and is created via the Slicer 3D software. We would like to able to automatically create 3-D views directly from WADO viewer.

Second, the completed eFolder system with IHE post-processing workflow needs to be evaluated in a real clinical setting. Performance evaluations and user feedbacks will be used to improve system performance and GUI design. The current GUI can be more interactive to

include dynamic referencing on individual lesions in WADO viewer and DICOM-SR viewer. Additional features will be discussed and planned according to user feedback.

4. Conclusions

In this paper, we present the design and development a comprehensive imaging-informatics based eFolder system for multiple sclerosis. It combines the concept of electronic patient record along with disease-centric database design, MR images, and an automated lesion quantification tool for an easier, more efficient system for longitudinal disease tracking, decision support, data mining, and data repository for both MS clinical and research environments. The eFolder system is capable of aiding the comparison studies between Hispanic-American and Caucasian MS patients via integrating MRI and clinical findings. The system is DICOM-complaint, while being completely web-based to allow remote access and telemedicine. MS lesions are identified and contoured by expert neuroradiologists, and a lesion quantification system has been developed in MATLAB. Quantification results have been converted into DICOM-SR for DICOM-compliant long-term storage. System workflow, based on IHE, has been developed and tested in a laboratory environment. Imaging data and patient disease data have been collected, while a graphical user interface has been developed to bring ease of access and user-friendliness to the MS eFolder. While complete integration is ongoing and several improvements are being refined, the eFolder concept aims to improve on MS diagnosis, tracking, and research. The eFolder will bring a novel and comprehensive approach to observe longitudinal MS lesion changes in MR, and deciding treatment plans that best suit the MS patient's profile.

Acknowledgments

Kevin C. Ma and James R. Fernandez were supported by NIH NIBIB T32 EB00438 Training Grant. Mark S. Shiroishi was partially supported by SC CTSI (NIH/NCRR/NCATS) Grant # KL2TR000131.

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Abbreviations

CNS	central nervous system
CSF	cerebral-spinal fluid
DICOM	digital imaging and communication in medicine
EDSS	expanded disability status scale
ePR	electronic patient record
FLAIR	fluid attenuated inverse recovery
GUI	graphical user interface
IHE	integrating the healthcare enterprise
HTTP	hypertext transfer protocol
LAC	Los Angeles county hospital
MRI	magnetic resonance imaging
MS	multiple sclerosis

PACS	picture archiving and communication system
PHP	PHP hypertext preprocessor
SC	secondary capture
SR	structured reporting
UID	unique identification
USC	university of Southern California
WADO	web-accessible DICOM object
WAMP	windows/Apache/MySQL/PHP
XML	extensible markup language

Fig. 1.

Three axial brain images of an MS patient. The left-most image is T1-weighted, the middle image is T2-weighted, and the right-most image is FLAIR. White regions in FLAIR image (as pointed by arrows) indicates MS lesions in white matter.

Fig. 2. Modular diagram of Multiple Sclerosis (MS) eFolder system. SR: structured reporting; DICOM: Digital Imaging and Communications in Medicine.

Fig. 3. General database schema for the MS eFolder. Arrows indicate how each table is related to each other in the schema.

Fig. 4.

DICOM-SR template used for the image processing module for the eFolder, as published by Le, A. (2009). [17] The figure shows the tree structure that can be stored in DICOM-compliant file structure.

Fig. 5. Workflow diagram for DICOM-SR conversion and display. Top row: converting MS quantification results to DICOM-SR for storage. Bottom row: querying and displaying information within DICOM-SR objects.

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Fig. 6.

XML document to store MS lesion quantitative analysis results based on DICOM SR template.

Fig. 7. Screenshot of comprehensive MS eFolder web-based GUI. Left panel: patient's clinical and demographic data. Right top panel: WADO image viewer embedded in eFolder GUI. Right bottom panel: SR document content in tabulated format.

Fig. 8. Screenshot of WADO viewer displaying DICOM images and DICOM-SC for the MS eFolder. Upper left panel displays the 2D contour overlay, upper right panel displays the 3D lesion rendering from different angles by the Slicer 3D software.

Fig. 9.
MS eFolder workflow diagram with IHE postprocessing profile. The steps 1 through 5 indicates the order of workflow of the demonstration.

Fig. 10. MS eFolder components diagram. The entire system includes 3 hardware components (Windows-based personal computers) and a closed network for demonstration purposes.

Serial No.	Patient ID	Patient Name	Study ID	Status
1	ID9067	PATIENT9067	6	Uploaded
2	ID9066	PATIENT9066	7	Uploaded
3	ID9058	PATIENT9058	8	Uploaded
4	ID9057	PATIENT9057	9	Uploaded
5	ID9056	PATIENT9056	10	Sent to CAD for Processing
6	ID9059	PATIENT9059	15	CAD Processing Complete

Fig. 11.

Status tracking page for MS eFolder post-processing workflow after a study (Study ID 10) has been sent to the post-processing (CAD) workstation, and after another study (Study ID 15) has been processed and sent back to the server.

MULTIPLE SCLEROSIS QUESTIONNAIRE

Study ID number: _____

Today's Date: ____/____/____

Directions: Read and answer the short-answer questions in the space provided. You may also answer with a check mark and/or circle all the answers that may apply. We have tried to make the questions quite specific. If, however, some confusion should arise, feel free to ask any research team member. We sincerely appreciate your participation.

I.- PARTICIPANT INFORMATION:

Name: _____

Date of Birth: _____

Gender: ☐ Male ☐ Female

Please circle: Right handed or Left handed or Ambidextrous

II.- SOCIAL HISTORY:

a) Birth Place: _____

b) Residence for age under 15 yrs: _____

c) Time in the United States: _____

d) Family Generation: _____

e) Type of Residence: ☐ Rural or ☐ Urban
 f) Highest level of education: ☐ Elementary ☐ Middle School ☐ High School
☐ College ☐ Post Graduate

g) Occupation:

Present: _____ Past: _____

h) Have you been exposed to pesticides? ☐ Yes or ☐ Noi) Do you smoke? ☐ Yes or ☐ No If Yes, for how many years? _____**Fig. 12.**

First out of 6 pages of Multiple Sclerosis questionnaire to collect patient data.

Fig. 13.
Scatter plot of total lesion volume between Caucasian and Hispanic patients.

Fig. 14.

Lesion volume of 4 patients, each with 4 studies from 2009 to 2014. Each dot represents a CAD result showing the overall lesion volume for that study.

Fig. 15.

Lesion contours from two separate studies superimposed on the same image. Red/darker contour is from a study in 2011, and green/lighter contour is from 2014. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)