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Database integration of protocol-specific neurological imaging datasets

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ABSTRACT

For many years now, Magnetic Resonance Innovations (MR Innovations), a magnetic resonance imaging (MRI) software development, technology, and research company, has been aggregating a multitude of MRI data from different scanning sites through its collaborations and research contracts. The majority of the data has adhered to neuroimaging protocols developed by our group which has helped ensure its quality and consistency. The protocols involved include the study of: traumatic brain injury, extracranial venous imaging for multiple sclerosis and Parkinson's disease, and stroke. The database has proven invaluable in helping to establish disease biomarkers, validate findings across multiple data sets, develop and refine signal processing algorithms, and establish both public and private research collaborations. Myriad Masters and PhD dissertations have been possible thanks to the availability of this database. As an example of a project that cuts across diseases, we have used the data and specialized software to develop new guidelines for detecting cerebral microbleeds. Ultimately, the database has been vital in our ability to provide tools and information for researchers and radiologists in diagnosing their patients, and we encourage collaborations and welcome sharing of similar data in this database.

Introduction

The wealth of information embedded in any given set of neuroimaging data is well beyond what is usually extracted in a single study. While the acquisition scheme itself might be fixed for different protocols, the data can be processed (either immediately or in a subsequent analysis) in many ways to look for different imaging biomarkers based on the study's objectives. Our own work has focused on neurological diseases, and over the years, we have established a number of protocols for detecting microbleeds and imaging iron in traumatic brain injury (TBI) and more recently, stroke patients. We began by collaborating with sites both nationally and internationally, and it became critical to design a data sharing repository to allow proper storage and extraction of data as needed for data analysis. In 2005, we were awarded state funding from the State of Michigan Technology Tri-Corridor fund to build a robust database to allow safe data storage and easy access to what is currently an expensive process to collect and maintain data if done by grant funding. Our goal was to establish several specific protocols and begin collecting data for diseases such as Alzheimer's disease (AD), specifically vascular dementia, multiple sclerosis (MS), Parkinson's disease (PD), stroke and TBI.

Our focus in the past has been to develop new MR technology via novel imaging sequences and image processing methods. The biggest challenge has been to test these ideas clinically with sufficiently large number of cases to have an impact on the field. We envisioned this repository to serve as a national database repository of de-identified data for the best possible MR data from different imaging centers, hospitals and research institutions (all shared and protected following the Health Insurance Portability and Accountability Act (HIPAA) regulations). Once the database was established, it could then be made available for reproduction of the same study anywhere, as well as for reprocessing and re-analyzing, data mining, and more in-depth statistical analysis as new image processing methods were developed (Greicius et al., 2004). This database was further expanded in 2010 to include collaborations with national and international investigators, who agreed to share their data as part of the current MR imaging repository. To date, based on images from this database, our group has published more than 100 papers, which otherwise would not have been possible.

MR Innovations employs its MR imaging patents, MR image processing software, and expert knowledge to provide quantitative and diagnostic data analysis tools and services to hospitals, neuroradiologists, and imaging centers, offering consulting, protocol optimization, collaborations, technical reporting for imaging centers, and original research publications. More recently, MR Innovations is taking advantage of the availability of this database by doing large-scale contract research for pharmaceutical companies. Over the past few years, our group has

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collaborated with many sites, many of whom have signed an agreement allowing us to store, use and share the data for future studies.

The database: Current status

Generally, the purpose of the database is to: a) keep large quantities of standardized data organized; b) maintain original and processed data in an easy to use format; and c) encourage sharing and research collaborations both publicly and privately. Our "Process Scheme for MR Innovations" (Fig. 1), in general, closely resembles the "Stages of Electronic Data Capture" as graphically described by Poline et al. (Poline et al., 2012): First the experiment is established and imaging protocols are designed or used with fixed acquisition parameters, images are collected from subjects from the MR scanner, or the data are transferred to us by a vendor who has adopted our protocol and ultimately stored on our servers. Then the raw data is de-identified and converted to a usable DICOM (digital imaging and communications in medicine) format. The server then pre-processes the data with myriad algorithms which may include sorting, anonymization, brain extraction, etc. After that, the database is populated with the acquisition parameters and remaining patient information on the server. The individual processors or researchers then perform any further processing on their workstations if needed and the quantified data are analyzed, reviewed, and prepared for technical reports or for research publications. The final processed de-identified data are uploaded back to the server for storage and potential future analysis. Any publications are then distributed through web services and databases such as PubMed Central or ScienceDirect.

The data

The database was originally developed to store MRI data that were collected for many different neuroimaging studies. This data was composed of a wide range of MRI sequences including conventional (heavily used in clinics – such as T1 and T2 – weighted imaging, Fluid Attenuated Inversion Recovery (FLAIR), proton density) and non-conventional approaches (such as susceptibility weighted imaging (SWI), perfusion weighted imaging (PWI), diffusion tensor imaging (DTI), functional MRI (fMRI), phase contrast flow quantification (FQ) and MR angiography and venography (MRAV)) for imaging the brain's structure, function, and composition. After this initiative, more data was added to the database from different centers outside our direct collaborations who adopted our image acquisition protocols, creating a large source of re-usable data (with proper permissions).

The current database holds MR data from more than 4000 cases, covering a spectrum of neurodegenerative diseases (dementia, migraine, AD, MS, PD, stroke and TBI) as well as a repository of data from healthy controls. Most of the collected data followed a single protocol for each disease, which made the quality and format of the data and processed results consistent and reliable between sites. For instance, in 2010, we developed a protocol to collect MRI data to best diagnose the damage in TBI. This paper resulted from a special workshop sponsored by the National Institutes of Health (NIH) and the United States military which is published in the Journal of Magnetic Resonance Imaging (Haacke et al., 2010) and has been adopted as the standard imaging protocol by the United States military (DCoE Clinical Recommendation, 2013).

The resurgence of a vascular hypothesis for MS occurred in 2009 (Zamboni et al., 2009). Demand by both researchers and patients for MRI scans (as well as ultrasound and selective catheter venography) to investigate extracranial venous structure and function (flow) increased. Though shorter MRI protocols with conventional MR imaging already existed for MS, we created a specialized venous imaging protocol which included phase contrast flow quantification, 2D time-of-flight venography, 3D contrast-enhanced Time Resolved Imaging of Contrast Kinetics (TRICKS) angiography, and SWI (Utriainen et al., 2012a, 2012b). More advanced tiers for this protocol included DTI and PWI using a T1-shortening contrast agent. Numerous institutions worldwide have adopted these protocols and have sent their standardized data to MR Innovations for flow processing and angiography review for venous anomalies (Table 1). This unique repository has grown to over 2000 cases all collected with a similar protocol. Several papers have been published related to the data from these sites (Utriainen et al., 2012a,2012b; Dake et al., 2011; Feng et al., 2012a,2012b; Haacke, 2011; Haacke et al., 2012a,2012b; Liu et al., 2014; Rahman et al., 2013; Sethi et al., 2014) (for more specific protocol information, visit http://mrinnovations.com/index.php?site=protocols). Collaborators from all the major vendors have participated in this program. Table 1 shows a list of de-identified data from some institutions that

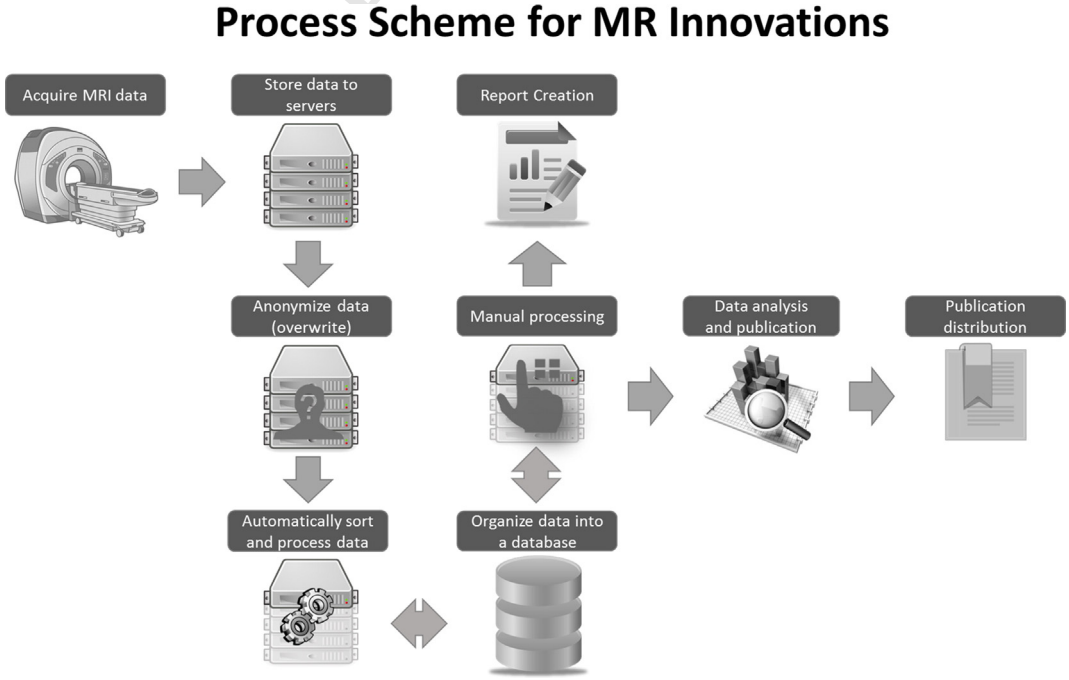

Fig. 1. Process scheme for MR Innovations.

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