Neuroimaging in Iran: A Review

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ABSTRACT

Neuroimaging allows noninvasive evaluation of the anatomy, physiology, and function of the brain. It is widely used for diagnosis, treatment planning, and treatment evaluation of neurological disorders as well as understanding functions of the brain in health and disease. Neuroimaging modalities include X-ray computed tomography (CT), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG). This paper presents an overview of the neuroimaging research in Iran in recent years, partitioned into three categories: anatomical imaging; anatomical image analysis; and functional imaging and analysis. Published papers reflect considerable progress in development of neuroimaging infrastructure, hardware installation and software development. However, group work and research collaborations among engineers, scientists, and clinicians need significant enhancement to optimize utility of the resources and maximize productivity. This is a challenge that cannot be solved without specific plans, policies, and funding.

1. Introduction

Neuroimaging refers to techniques that either directly or indirectly image the structure or function of the nervous system (mainly brain) in vivo. It is a relatively new discipline within medicine and neuroscience, emerged from the improvements in the medical imaging systems and computer hardware and algorithms. Nowadays, medical imaging systems including X-ray computed tomography (CT), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), and positron emission tomography (PET) are used to provide insight into the anatomical structure and functional organization of the brain. In addition, signal acquisition systems like electroencephalography (EEG) and magnetoencephalography (MEG) are used to generate temporally resolved information about the brain function.

The growing interest for the exploration and understanding of the human nervous system and especially the brain is the main motivation behind the expansion and progress of the neuroimaging around the world. Humans benefit from neuroimaging to mimic the brain via artificial intelligence and improve diagnosis and treatment of neurological diseases. In concert with the rest of the world, researchers and physicians in Iran have developed infrastructure for clinical evaluations and research studies as well as education in this exciting field.

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Scientific papers are widely used in the world as indicators of the research activities. As such, we have explored the journal papers (mostly ISI) published by authors from Iran to identify related research activities in the country. We hope this presentation helps future research plans and collaborations in the field. We also hope that it benefits strategic planning and funding that would improve neuroimaging activities throughout the country.

2. Methods

The "ISI Web of Knowledge" and Scopus were under pinned for the search of Iranian researchers' publications in Neuroimaging. The keywords used for the search were: neuroimaging, fMRI, MRI <AND> Brain, CT <AND> Brain, and PET <AND> Brain. The number of records found in each search is reported in Table 1. Although the relevance of all papers, identified by the searches, to neuroimaging is not the same, the fourth column of this table may give a rough estimate of the popularity of the neuroimaging methods in Iran.

Table 1. Statistics of the initial searches.

	Keywords Used besides Iran for Search	Database	Number of Records
1	Neuroimaging	Scopus	121
2	fMRI	ISI Web of Knowledge	31
3	MRI <AND> Brain	ISI Web of Knowledge	108
4	CT <AND> Brain	ISI Web of Knowledge	64
5	PET <AND> Brain	ISI Web of Knowledge	12

After the search, the results were assessed by reading the abstracts one by one; unrelated and duplicate papers, conference papers, and case reports were excluded. The remaining papers were then categorized based on their main focus. Three study categories emerged from this exploration: anatomical imaging, anatomical image analysis, and functional imaging. Table 2 shows the number of records in these categories. In the next section, we present an overview of the papers in each category to provide an outlook to the current state of research in each category.

Table 2. Statistics of the journal papers reviewed in each of the categories.

	Anatomical Imaging	Anatomical Image Analysis	Functional Imaging and Analysis
Number of papers	24	35	26

3. Results

3.1. Anatomical Imaging

Medical imaging modalities used for imaging the brain anatomy are key tools for diagnosing and treatment of many neurological disorders. As Palesh et al. (2008) have reported, neurosurgeons, orthopedists, and neurologists have contributed to more than 88% of the MRI utilization in the country. The spinal column (55%), brain (26%), and knee (11%) have been the most common organs scanned by MRI. Many research works have emerged using MRI and CT images as described below.

• **Evaluation of Head Injury:** Different groups have shown the value of CT images for the diagnosis and follow up of the head injury (Aarabi 1995, Faraji et al. 2005, Saboori et al. 2006, Khaji et al. 2006, Etemadrezaie et al. 2007, Iranmanesh et al. 2009).

• **Early Diagnosis of Vascular Damage:** Karimi et al. (2010) used MRI to monitor early asymptomatic or subclinical vascular damage in the brain to determine the incidence of brain ischaemia in patients with beta-thalassaemia intermedia.

• **Diagnosis and Evaluation of Brain Tumors and Multiple Sclerosis (MS):** Contrast enhanced MRI using Gadolinium DTPA has been used for the evaluation of brain tumors and multiple sclerosis lesions (Bagheri et al. 2008). New methods using the magnetically labeled particles are being developed for molecular MRI to identify glioma and other lesions (Arbab et al. 2007, Rad et al. 2007). Ashjazadeh et al. (2003) studied Neuro-Behcet's disease, a masquerader of MS, using MRI. Borazanci et al. (2009) described the relation between clinical features, pathophysiology, and neuroimaging features in MS patients and how neuroimaging assists physicians in a more accurate diagnosis of MS versus its imitators. Etemadifar et al. (2009) studied the relationship between MS and neurofibromatosis type 1 whereas Kalanie et al. (2009) studied opticospinal MS using MRI. Ashtari et al. (2010) compared clinical and MRI features of early-onset MS vs. adult-onset MS.

• **Diagnosis and Evaluation of Stroke:** Ghandehari et al. (2008) used CT and MRI to study the cause of posterior circulation syndrome while Mousavi et al. (2007) compared anterior circulation stroke with posterior circulation stroke. Nematbakhsh et al. (2008) used MRI to evaluate correlation between nitric concentration and lesion size in stroke.

• **Diagnosis and Evaluation of Epilepsy:** Khodapanahandeh et al. (2006) used MRI and CT for diagnosis of epilepsy in children while Fallah et al. (2007) used them in their comparison of intravenous lidocaine and midazolam infusion for refractory convulsive status epilepticus in children. Taghdiri et al. (2009) used MRI to evaluate the treatment effects for reversible posterior leukoencephalopathy syndrome.

3.2. Anatomical Image Analysis

Image analysis of the anatomical images of the brain constitutes a considerable fraction of neuoimaging researches in Iran, as summarized below.

• **Brain Segmentation:** This category can be partitioned into two subcategories: tissue segmentation; and structure segmentation. For tissue segmentation, Soltanian-Zadeh et al. (1997) used multi-resolution analysis to segment brain tissues from skull and scalp. Soltanian-Zadeh et al. (1998a) developed mathematical methods that use multi-parametric MRI to segment different regions of brain tumors from normal tissues. Their method is capable of estimating partial volumes of homogeneous tissues in each voxel. Hasanzadeh et al. (2008) used fuzzy segmentation and membership connectedness for this purpose while Forouzanfar et al. (2010) used fuzzy c-means clustering along with neighborhood attraction.

For segmentation of the brain structures like the hippocampus, Ghanei et al. (1998; 2002) developed two-dimensional (2D) and three-dimensional (3D) deformable models. Amini et al. (2004) integrated fuzzy clustering and dynamic contours to segment the thalamus in brain MRI. These methods require operator to draw an initial contour on the structure of interest. To alleviate this need, Siadat et al. (2007) developed a knowledge-based system, using an expert system, to localize brain structures automatically. Akhundi-Asl et al. (2009) and Bijari et al. (2010) developed shape models based on general symmetry of the brain and the relation among the brain structures while Jabarouti et al. (2009) used geometric moment invariants and neural networks for this purpose. Nazem-Zadeh et al. (2010) developed an atlas-based algorithm for segmentation of fiber bundles from diffusion tensor MRI.

• **Quantitative Evaluation of Brain Structures:** To evaluate gender differences and age-related morphometrical changes of the thalamus, interthalamic adhesion, and the right-left differences of the thalamus, Mohammadi et al. (2008) measured the related dimensions on MRI. Similarly, to determine the dimensions of different parts of pons and compare the data in accordance with age and sex, Rajaei et al. (2009) measured the related dimensions on MRI. Likewise, Javadapour et al. (2010) estimated the hippocampal volumes of bipolar disorder patients and sex-, age-, and education-matched comparison subjects on MRI.

• **Analysis of Multispectral and Multi-Modality Data:** In most MRI studies, images with T1, T2, and proton density weightings are acquired. To analyze them together and benefit from the multi-dimensional feature space defined by them, Soltanian-Zadeh et al. (1996) developed an optimal transformation. This method maps the original data into a three-dimensional (3D) feature space in which normal tissues are clustered on predefined locations and abnormalities are clustered elsewhere. The authors have shown that this method distinguishes recurrence tumor in the brain from edema and radiation necrosis (Soltanian-Zadeh et al. 1998a). They have also shown that it identifies different regions of the brain tumors, useful for guiding biopsy of the tumor (Soltanian-Zadeh et al. 1998b). The concept has also been extended to analyze images of the stroke patients in order to differentiate salvageable tissue form dead one in the brain and predict the final lesion volume (Jacobs et al. 2001). To overcome limitations due to the field nonuniformity, Roozbahani et al. (2000) have developed an adaptive algorithm based on statistical modeling and finite mixtures. Daneshvar et al. (2007; 2010) developed a multi-scale algorithm based on retinal model to fuse MRI and PET data optimally. Their method maximizes spatial features of MRI and functional features of PET in a combined image.

• **Image Registration:** To compare images acquired at different times or from different individuals, they must be co-registered. Also, to compare an image of the tissue to the tissue itself in animal studies, medical images and histological images must be co-registered. To this end, Jacobs et al. (1999) developed a semi-supervised algorithm to match MRI and histological images of the rat brain. Ghanei et al (2000) developed an unsupervised, boundary-based nonlinear registration (warping) algorithm to match different brain images. This and other algorithms may use landmarks to guide the deformation process. To this end, Fatemizadeh et al. (2003) developed an automatic landmark identification algorithm using artificial neural networks. Image registration can be used in the development of anatomical atlases. An example of such an application to develop an MRI atlas of neonatal brain is reported in Kazemi et al. 2007.

• **Finite Element Modeling (FEM):** To use images acquired before and during surgery for operational guidance, in addition to the registration of imaging and neuronavigator coordinate systems, deformation of the brain after opening of the skull should be measured or predicted. In this direction, Hamidian et al. (2009) proposed a method using finite element modeling of the brain to predict this deformation. To obtain an appropriate model of biomechanical behavior of brain tissue and deformation of ventricles, Farmanzad et al. (2007) developed a computerized plain strain finite element model. Saberi et al. (2007) used this model to study the degree of displacement and deformation of the ventricles in acute epidural hematoma. In another application, Behnia et al. (2008) simulated pressure and temperature distributions resulting from transdural ultrasound brain surgery by employing FEM for solving the Helmholtz and bioheat equations in the context of a two-dimensional MRI-based brain model.

• **Applications:** Nagesh et al. (1998) analyzed diffusion weighted images of the stroke patients to evaluate tissue evolution after stroke by following the time course of apparent diffusion coefficient (ADC) of the lesion. Soltanian-Zadeh et al. (2007) analyzed MRI of stroke patients to identify salvageable tissue. Siadat et al. (2005) developed a content based image database system to facilitate analysis of multi-modality neuroimaging data of epileptic patients along with their clinical data and test results. Khayati et al. (2008) developed algorithms to extract quantitative information from MRI of MS patients for objective evaluation and staging of the disease. Jafari et al. (2010) extracted quantitative information from MRI for noninvasive lateralization of temporal lobe epilepsy patients. Yahaghi et al. (2006) estimated concentration of contradictory agent in the tissue from MRI using mathematical modeling and Monte Carlo simulation.

3.3. Functional Imaging and Analysis

Basic, developmental, and applied researches on functional Imaging in Iran are summarized below.

• **Basic fMRI:** The focus of the work in this field has been on activation detection in single subject and in multi-subjects as well as statistical analysis of the data. Wavelet transform (Hossein-Zadeh et al. 2003a), fuzzy clustering (Jahanian et al. 2004; 2005), adaptive spatial filtering (Hossein-Zadeh et al. 2003b), subspace modeling (Hossein-Zadeh et al. 2003c), and a model independent method (Soltanian-Zadeh et al. 2004) all deal with single subject activation detection. For group analysis of the fMRI data, Shams et al. (2006) proposed a method based on the testing of the correlation of the multi-subject fMRI data in a signal subspace, whereas Soleymani et al. (2009) used random and fixed effects in the wavelet domain. Statistical analysis of the fMRI data has also been conducted through Bayesian signal detection (Rohani et al. 2006) and dealing with the fractal noise (Afshinpour et al. 2008) and random fields (Shafie 2003). These methods focus on the statistical features of the fMRI time series.

• **Applied fMRI:** In these studies, researchers have investigated the activated areas by motor task (Harirchian et al. 2010), Farsi word generation (Mahdavi et al. 2006; Mahdavi et al. 2008; Mahdavi et al. 2010), visual task (Mirzajani et al. 2007), effect of aging on resting state (Batouli et al. 2009), evaluation of activation areas in Alzheimer patients (Oghabian et al. 2010) as well as other brain functions (Naghavi at el. 2007; Naghavi 2009).

• **Basic PET Imaging:** Jalilian et al. (2008) developed a tracer for PET imaging. Moghaddam et al. (2009) designed and simulated a spherical PET system for brain imaging.

• **Applied SPECT:** Eftekhari et al. (2005) investigated the activated areas in the subjects with post-traumatic smell impairment using SPECT. Atighechi et al. (2009) detected post-traumatic loss of smell and the areas in the brain that are related to olfactory impairment using SPECT and MRI.

• **Basic MEG:** As MEG provides time resolved information of brain activity with poor spatial resolution, its joint analysis with fMRI (which provides high spatial resolution) has been a subject of interest. Research work has been done on MEG analysis as well as integration of MEG and fMRI (Babajani et al. 2005; Babajani et al. 2006; Babajani et al. 2008; Babajani et al. 2010). They mostly deal with the development of an integrated model for joint analysis of MEG and fMRI.

It should be noted that we have not included the researches on EEG, as they contain a vast variety of signal processing techniques and applications from brain computer interface (BCI) to event related potentials (ERP) and data classification, many of which are not considered as neuroimaging investigations.

4. Discussion

Based on a comprehensive search, we explored the main categories of the neuroimaging studies in Iran. Although the field is a relatively new and requires collaborations among different experts, Iranian scientists have managed to make valuable contributions. Yet, their contributions have been restricted to a subset of areas explored internationally. Analytical developments and basic research on the analysis of neuroimages have been conducted at the international level but their applications to the clinical studies have not been as vast and thus need to grow. Moreover, the work dealing with the development of new hardware has been quite limited. The same is true for the development of MRI contrast agents as well as diffusion, perfusion, and spectroscopic imaging using MRI.

Our study shows that some of the building blocks required for an infrastructure to conduct research and clinical applications of novel neuroimaging technologies in the country exist. There is a good number of imaging systems in the country and there are experts working in the related fields. However, strong team work, enhanced coordination, and substantial research funding are essential to complete the infrastructure and boost the activities in this exciting field.

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