



Online molecular image repository and analysis system: A multicenter collaborative open-source infrastructure for molecular imaging research and application



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ABSTRACT

Molecular imaging serves as an important tool for researchers and clinicians to visualize and investigate complex biochemical phenomena using specialized instruments; these instruments are either used individually or in combination with targeted imaging agents to obtain images related to specific diseases with high sensitivity, specificity, and signal-to-noise ratios. However, molecular imaging, which is a multidisciplinary research field, faces several challenges, including the integration of imaging informatics with bioinformatics and medical informatics, requirement of reliable and robust image analysis algorithms, effective quality control of imaging facilities, and those related to individualized disease mapping, data sharing, software architecture, and knowledge management.

As a cost-effective and open-source approach to address these challenges related to molecular imaging, we develop a flexible, transparent, and secure infrastructure, named MIRA, which stands for Molecular Imaging Repository and Analysis, primarily using the Python programming language, and a MySQL relational database system deployed on a Linux server. MIRA is designed with a centralized image archiving infrastructure and information database so that a multicenter collaborative informatics platform can be built.

The capability of dealing with metadata, image file format normalization, and storing and viewing different types of documents and multimedia files make MIRA considerably flexible. With features like logging, auditing, commenting, sharing, and searching, MIRA is useful as an Electronic Laboratory Notebook for effective knowledge management. In addition, the centralized approach for MIRA facilitates on-the-fly access to all its features remotely through any web browser. Furthermore, the open-source approach provides the opportunity for sustainable continued development.

MIRA offers an infrastructure that can be used as cross-boundary collaborative MI research platform for the rapid achievement in cancer diagnosis and therapeutics.

1. Introduction

Molecular imaging (MI) is defined as the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in humans and other living systems [1]. MI has been considerably useful in the fields of diagnostics, therapy monitoring, drug discovery, and drug development, and is a promising tool for understanding nanoscale reactions such as protein-protein interactions and enzymatic conversion [2]. To visualize and investigate complex biological phenomena at the molecular and cellular levels, MI researchers and

clinicians require specialized instruments and techniques, which are used either individually or in combination with targeted imaging agents. These specialized techniques are mainly various imaging modalities, such as Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT), Magnetic Resonance Imaging (MRI), Computed Tomography (CT), PET-CT, SPECT-CT, PET-MRI, Ultrasonography (USG), and Near Infrared Spectroscopy (NIRS) (Fig. 1); these techniques are used to detect biomarkers or capture biochemical and cellular processes related to diseases with high sensitivity, specificity, and signal-to-noise ratios [3].

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Though this translational research field is very promising [1–9], it is also very challenging [3–5] mainly because of its interdisciplinary nature [2]. To obtain promising results from MI research while addressing the interdisciplinary challenges, a collaborative, transparent, and flexible framework is required, which can bridge the knowledge gaps among researchers from different disciplines by combining their expertise and skills. In addition, there exist several challenges in imaging informatics, such as integration of imaging informatics with bioinformatics and medical informatics, requirement of reliable and robust image analysis algorithms, quality control of imaging facilities, and those related to individualized disease mapping, data sharing, and appropriate software architecture [10]. To address these challenges, an image storage and information database is required to link various stages of research in order to achieve the desired goal. Such a framework should include reusable modules, should be scalable and sustainable for continued development, and be interoperable with other software systems. Therefore, open-architecture and open-source image information systems are an ideal solution for these requirements [10].

Although there exist several open-source medical imaging informatics tools, such as XNAT [11], LORIS [12], LONI [13]; and clinical trials management system (CTMS) [14] for clinical research and application, none of these is a one-size-fits-all approach solution for MI research. In this study, we develop a one-size-fits-all approach solution for MI research, which is an open-source collaborative, flexible, transparent, and secure online MI repository and analysis infrastructure named MIRA, to bridge the knowledge gaps among researchers by combining interdisciplinary or multidisciplinary research outcomes of MI research. MIRA is designed with a centralized image archiving infrastructure and information database so that a multicenter collaborative informatics platform can be built. Because this infrastructure should meet the demands of multidisciplinary MI research, the system must be quite flexible; therefore, it should have flexibility and efficiency in data entry, image file format normalization services to convert between various image formats, ensuring that different types of documents and multimedia files can be stored and viewed. In addition, it is important to integrate imaging informatics tools with other bioinformatics and medical informatics tools to provide a comprehensive approach to associate imaging data with

other scales of molecular and clinical data types, called metadata [10]. Finally, to address challenges of transparency, accountability, and knowledge management [15], MIRA is designed based on the concept of an electronic laboratory notebook (ELN) [16–18].

2. Materials and methods

To ensure that our infrastructure is cost-effective and open-source, MIRA is designed with freely available software without compromising security; moreover, a Linux based server and computer system are used. In addition, most program codes are written in the Python [19] programming language with the Pylons [20] web framework. In particular, PyBLD [21] is utilized for data analysis and image manipulation. In some of the cases, for fast computation, like for molecular image conversion and analysis, program codes are written in the C programming language. Furthermore, JavaScript is used for some interactive convenience. A MySQL [22] database engine is used for data storage and manipulation. Thus, no proprietary software was used in the development of MIRA.

2.1. Technical overview

The basic architecture of MIRA is the widely used three-tier design [23] that includes a RDB backend, a Python middleware, and a web-based user interface (Fig. 2).

2.2. Design of MIRA

The conventional Hospital Information System (HIS), Radiology Information System (RIS), and Picture Archiving and Communication System (PACS) have a long developmental history starting in the 1960s [24]; in modern times, these systems have become ubiquitous in a hospital; however, these systems do not fulfil the requirements of MI research because of the conceptual differences in organizing data between daily hospital routines and in the case of MI studies (Table-1). In addition, the commercial HIS/RIS/PACS are prohibitively expensive for researchers.

In general, MI research is project-based, where multidisciplinary or

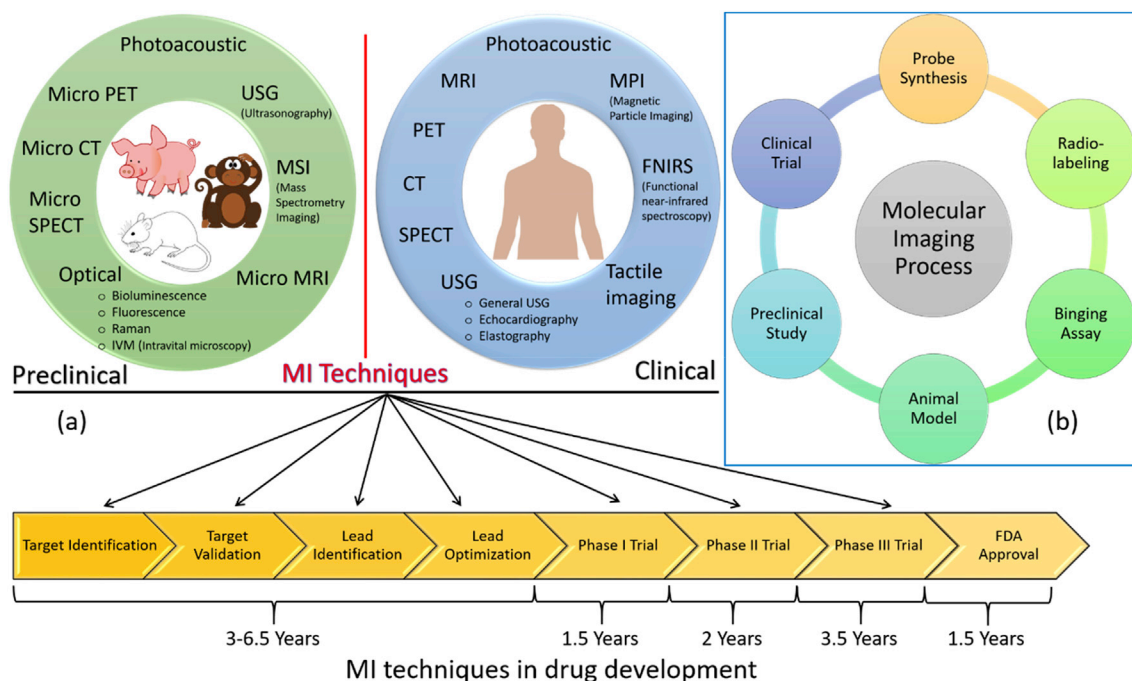


Fig. 1. (a) New drug development process. It is a considerably long process (10–15 years); however, this process can be accelerated using MI techniques at every stage of drug development. (b) Overall process of new probe development in MI research.

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