
CLINICAL RESEARCH: MEDICAL IMAGE PROCESSING, ANALYSIS, AND VISUALIZATION

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ABSTRACT

Imaging plays a crucial role across various medical and laboratory disciplines, from cellular studies with 3D confocal microscopy to virologists reconstructing viruses from micrographs and radiologists identifying tumors in MRI and CT scans. Neuroscientists also utilize imaging for detecting metabolic brain activity. Formerly reliant on expensive UNIX workstations and custom software, the analysis and visualization of diverse image types can now be performed on cost-effective desktop computers. This paper introduces MIPAV (Medical Image Processing Analysis and Visualization), a platform-independent program tailored for the Internet-linked medical research community. MIPAV facilitates clinical and quantitative analysis of medical images over the Internet, enabling remote researchers and clinicians to collaborate seamlessly, enhancing their capabilities in studying, diagnosing, monitoring, and treating medical disorders.

Index Terms *Internet of Things (IoT), Edge/cloud computing, Time-Sensitive Networks (TSN), Machine Learning.*

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Biographical notes:

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1. INTRODUCTION

The National Institutes of Health (NIH) has played a pivotal role in advancing medical research and technology, and one of its notable contributions is the development of MIPAV (Medical Image Processing Analysis and Visualization). MIPAV stands out as a versatile and extensible image processing and visualization program that caters to the complex needs of researchers and practitioners in the field of medical imaging.

At its core, MIPAV is designed to be n-dimensional, meaning it can handle data from various medical imaging modalities that produce multidimensional datasets. This capability makes it a powerful tool for analyzing and visualizing diverse types of medical images, including those generated by techniques such as magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and more. The platform-independent nature of MIPAV ensures its compatibility with different operating systems, making it widely accessible to researchers across various computational environments.

MIPAV serves a dual purpose by functioning both as an end-user application and an Application Programming Interface (API). As an end-user application, MIPAV provides a comprehensive suite of basic and advanced image analysis and visualization tools. These tools empower researchers and medical professionals to perform a wide range of tasks, from simple image viewing and segmentation to more complex quantitative analyses. The user-friendly interface makes it accessible to those without extensive programming skills, enabling a broader audience to leverage its capabilities for their research.

For researchers with programming skills and image processing knowledge, MIPAV serves as an API, offering the flexibility to develop custom analysis or visualization components through its plug-in feature. This extensibility is a key feature that sets MIPAV apart, allowing users to tailor the software to their specific research needs. By fostering a community of developers and encouraging the creation of plug-ins, MIPAV becomes a dynamic and evolving platform capable of addressing emerging challenges and incorporating cutting-edge techniques in medical image analysis.

The plug-in architecture also facilitates collaboration and knowledge exchange within the research community. Researchers can share their custom algorithms, analysis methods, or visualization techniques as plug-ins, fostering a collaborative ecosystem that accelerates progress in the field of medical imaging.

2. OVERALL DESIGN

MIPAV (Medical Image Processing Analysis and Visualization), a powerful tool developed by the National Institutes of Health (NIH), stands at the forefront of medical imaging research, designed with a modular structure and leveraging the object-oriented features of Java. This versatile platform is tailored to meet the diverse imaging requirements of the NIH intramural research community, offering cross-platform execution, support for various image formats, advanced Volume of Interest (VOI) handling, extensibility through plug-ins, and robust visualization capabilities for 2D, 3D, and 4D datasets.

<p><u>Views</u> (2D planar, tri-planar, “lightbox”, cine, 3D surface)</p>	<p><u>VOIs</u> 32K Unique VOIs</p>	<p><u>Algorithms</u> (blurring, segmentation, gradient magnitude, boundary evolution, etc.)</p>
<p><u>Data (Image) types</u> N-Dimensional (Boolean, byte, unsigned byte, short, unsigned short, int, long, float, double, RGB, complex)</p>		
<p><u>File types</u> (Raw, Analyze, DICOM3.0, TIFF, GIF, PNM, JPEG, MINC, NetCDF, AVI, QuickTime)</p>		

Figure 1. Design Functional Overview of MIPAV

Modular Structure and Object-Oriented Design :

MIPAV's foundation lies in its modular structure and object-oriented design, both facilitated by the use of Java. This design choice enhances the software's flexibility, scalability, and maintainability. The modular architecture allows for the seamless integration of various components, making it adaptable to evolving research needs and ensuring a robust framework for future enhancements.

Functional Overview and Core Features:

Figure 1 provides a functional overview of MIPAV, emphasizing its core features. At its core, MIPAV is capable of handling n-dimensional data, making it suitable for a wide array of medical imaging modalities, including 2D, 3D, and 4D datasets from microscopy, X-ray, CT, MRI, fMRI, and PET. The software's versatility is further highlighted by its support for images up to four dimensions and various data types, ensuring compatibility with the diverse nature of medical imaging data.

Three fundamental functional blocks interface with the data buffer: Views, VOIs, and Algorithms. The Views module offers a graphical user interface for image viewing and manipulation, providing researchers with an intuitive toolset for examining and interacting with medical images. The VOIs module enables interactive segmentation and measurement, allowing users to define Volume of Interest for detailed analysis. The Algorithms module, comprising over 20 image processing and analysis tools, provides the necessary computational capabilities to extract meaningful information from medical images.

Key Features Addressing NIH Imaging Requirements

a. Cross-Platform Execution:

MIPAV's support for cross-platform or platform-independent execution is crucial for the NIH's diverse research involving a variety of image datasets. This includes 2D, 3D, and 4D datasets from different modalities such as microscopy, X-ray, CT, MRI, fMRI, and PET. The software's adaptability extends to the heterogeneous distribution of computer platforms, including Windows, Linux,

Macintoshes, SGI workstations, Sun Microsystems, and Hewlett Packard, ensuring accessibility and usability across different environments.

b. Image Access in Standard Formats:

Ensuring seamless access to images is vital for any image processing and analysis tool. MIPAV accomplishes this by supporting industry-standard image formats such as DICOM 3.0, Analyze, TIFF, and Raw. Its DICOM compliance enables remote access to clinical images via the DICOM interface, fostering interoperability and compatibility with diverse applications and medical equipment. This feature not only streamlines data input but also facilitates collaboration and data exchange across various platforms.

c. Volume of Interest (VOI) Handling:

MIPAV's robust Volume of Interest (VOI) handling capabilities contribute significantly to medical image segmentation. The software supports automatic, semi-automatic, or user-guided generation of VOIs, offering flexibility based on the user's preferences and the specific requirements of the research project. This feature aids in extracting quantitative information about various tissue types, laying the foundation for advanced image analysis and interpretation.

d. Extensibility with Plug-in and Macro Capability:

MIPAV's extensibility is a key strength, allowing researchers to tailor the software to meet the specific requirements of their projects. The plug-in architecture enables the integration of Java-based image processing components, empowering users to add custom functionalities seamlessly. Moreover, the development of a simpler MIPAV macro language further enhances the software's flexibility, enabling researchers to create and share macros for unique and specialized functionalities. This extensibility ensures that MIPAV can evolve alongside emerging research needs and technological advancements.

e. Visualization of 2D, 3D, and 4D Datasets:

MIPAV's visualization system is a cornerstone of its capabilities, offering a rich set of tools for rendering and interpreting medical images. The software is equipped to handle information from various datasets, providing tools such as surface rendering, composite displays, image magnification, rotation, color look-up tables, multi-planar views, and movies. The support for flexible and realistic 3D visualization is crucial for conveying information effectively, especially when dealing with complex datasets from diverse imaging modalities. This feature enhances the interpretability of results and facilitates better communication of findings within the research community.

3. APPLICATIONS OF MIPAV AT NIH.

In the realm of medical imaging research, the application of MIPAV (Medical Image Processing Analysis and Visualization) plays a crucial role in advancing understanding and treatment strategies for various neurological and ophthalmological conditions. Two specific instances highlight the significance of MIPAV in segmentation and visualization within the context of Alzheimer's disease research at the Geriatric Psychiatry Branch of the National Institute of Mental Health (NIMH) and the Phase I evaluation of a laser technique for choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD) at the National Eye Institute (NEI).

3.1. Geriatric Psychiatry Branch at NIMH: Alzheimer's Disease Research

Research Focus and Objectives:

The Geriatric Psychiatry Branch at NIMH focuses its efforts on Alzheimer's disease research, particularly in elderly patients. Alzheimer's disease is a progressive neurodegenerative disorder that predominantly affects older individuals and is characterized by cognitive decline and structural changes in the brain. Understanding the progression of the disease over time is crucial for developing effective diagnostic and therapeutic interventions.

Utilization of MIPAV:

MIPAV is employed at the Geriatric Psychiatry Branch for the segmentation and visualization of structural and functional MRI brain images. Structural MRI provides detailed information about brain anatomy, while functional MRI allows researchers to observe brain activity in real-time. MIPAV's capabilities are instrumental in analyzing these complex datasets.

Volume of Interest (VOI) Generation and Editing:

Multiple layers within MIPAV are utilized to generate and edit Volume of Interests (VOIs). This capability is crucial for isolating specific regions of interest within the brain, enabling researchers to quantify subtle changes in total brain volume and specific brain structures over a ten-year period. VOI editing tools in MIPAV facilitate fine-tuning of segmented areas, ensuring accuracy in the identification and measurement of structural changes.

Optimized Segmentation Algorithms:

MIPAV's segmentation algorithms are optimized for the removal of extraneous tissues, enhancing the precision of image analysis. The refined segmentation process aids in isolating relevant structures within the brain and contributes to the accuracy of the measurements taken over the longitudinal study period.

DICOM Header Information for Measurements:

MIPAV leverages information stored in the DICOM header for mensuration, allowing researchers to obtain total brain volume measurements. This approach provides standardized and reliable data, ensuring consistency across longitudinal studies. The integration of DICOM header information enhances the efficiency and accuracy of data extraction and analysis.

Significance for Alzheimer's Research:

The use of MIPAV in Alzheimer's disease research at NIMH is significant for tracking the progression of the disease and understanding how specific brain structures are affected over time. This knowledge is essential for developing targeted interventions and personalized treatment strategies for individuals with Alzheimer's disease.



Figure 2. Axial Image of Human Brain with VOIs for Skull and Tissue Removal Using Watershed Segmentation

3.2. National Eye Institute (NEI): Laser Technique for Choroidal Neovascularization (CNV) in AMD

Research Focus and Objectives:

The National Eye Institute (NEI) is conducting Phase I evaluation of a laser technique to address choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD). AMD is a leading cause of blindness in individuals over 60, and CNV is a critical aspect of its pathogenesis. The goal is to evaluate a laser-based therapeutic approach for treating CNV and preventing vision loss.

Utilization of MIPAV:

MIPAV is a crucial tool in the NEI's research, specifically for the analysis of images obtained through fluorescein (FA) and indocyanine (ICG) angiography. These imaging modalities capture intricate details of retinal and choroidal blood vessels, providing essential information for evaluating the efficacy of the laser technique.

Handling Varied Imaging Conditions:

Images obtained through FA and ICG angiography are captured at varying angles, magnifications, and with different filters. The diversity in imaging conditions poses a challenge for accurate analysis and comparison. MIPAV's capabilities are harnessed to address this challenge.

Image Registration and Superimposition:

MIPAV facilitates image registration and superimposition, aligning images captured at different wavelengths and angles. This capability is crucial for creating a comprehensive and integrated view of the retinal and choroidal vasculature. The accurate superimposition of images is essential for identifying and characterizing CNV and evaluating the success of the laser photocoagulation technique.

Significance for AMD Research:

The use of MIPAV in the NEI's research is significant for advancing our understanding of AMD and developing targeted therapeutic interventions. By leveraging MIPAV's image registration and superimposition capabilities, researchers can accurately assess the impact of laser-based interventions on CNV. This has direct implications for the development of innovative treatment strategies for AMD, a prevalent and debilitating condition affecting the aging population.

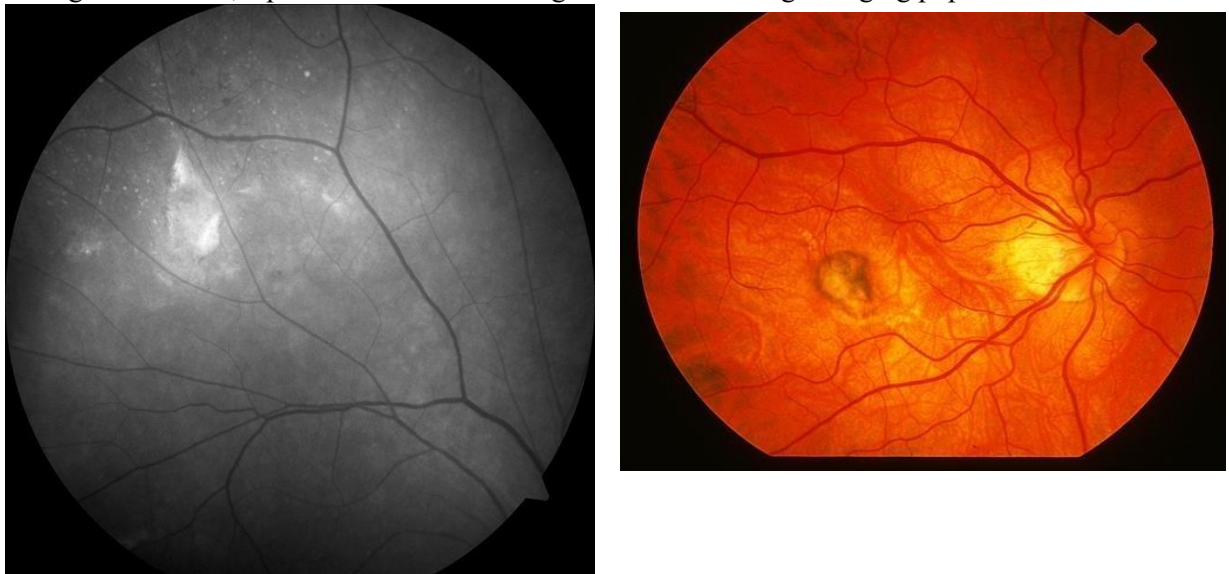


Figure 3. Retina Images with Manual Landmarks for Registration of CNV and AMD Using Leastsquares Algorithm

4. CONCLUSIONS AND FUTURE DECISIONS

The continuous development of MIPAV (Medical Image Processing Analysis and Visualization) reflects a commitment to meeting the evolving and diverse needs of the National Institutes of Health (NIH) user community. This platform-independent, n-dimensional, and extensible image processing application has made significant strides in providing advanced tools for medical image analysis. Ongoing efforts are centered on expanding functionalities to address emerging challenges and incorporate cutting-edge techniques, ensuring that MIPAV remains a valuable resource for researchers and clinicians.

One notable area of ongoing enhancement is the incorporation of various registration algorithms. Registration is a critical aspect of medical image analysis, enabling the alignment of images from different modalities or time points. The integration of diverse registration algorithms within MIPAV broadens its applicability and ensures its utility across a range of imaging scenarios. This enhancement is particularly beneficial for longitudinal studies, where the alignment of images over time is essential for tracking disease progression and treatment efficacy.

Surface rendering, another focus of current development efforts, adds a new dimension to visualizing medical images. By creating three-dimensional representations of anatomical structures, researchers and clinicians can gain deeper insights into the spatial relationships within the body. This

enhancement is valuable for surgical planning, educational purposes, and improving overall understanding of complex anatomical structures.

Future plans for MIPAV include the addition of volume rendering, an advanced technique that allows for the visualization of internal structures within a volume of data. This capability is especially relevant for medical imaging modalities such as CT and MRI, where three-dimensional reconstructions enhance the interpretation of intricate anatomical details. The incorporation of volume rendering will further expand MIPAV's capabilities, making it a comprehensive tool for advanced visualization in medical research.

In addition to rendering techniques, MIPAV is set to integrate advanced segmentation algorithms. Segmentation is a fundamental step in image analysis, involving the partitioning of an image into meaningful regions. The incorporation of sophisticated segmentation algorithms enhances MIPAV's ability to precisely identify and analyze specific structures or abnormalities within medical images. This is crucial for accurate diagnosis and quantitative analysis in various medical research applications.

Customization remains a key aspect of MIPAV's development strategy. The platform's extensible nature allows for the continual customization of components to address specific requirements identified by collaborators. This flexibility ensures that MIPAV can be adapted to the unique needs of different research projects and accommodates emerging trends and methodologies in medical imaging research.

The implementation of the MIPAV scripting language is a significant step towards automation and workflow efficiency. This scripting language enables users to automate repetitive tasks, streamlining the image processing and analysis pipeline. Automation not only improves efficiency but also reduces the likelihood of errors, enhancing the overall reliability of research outcomes. This feature is particularly beneficial for users dealing with large datasets or conducting repetitive analyses, allowing them to focus on more complex aspects of their research.

While MIPAV has historically focused on radiological imaging modalities, its adaptability extends to other datasets, including microarrays, microscopy images, and micrographs. This versatility broadens the scope of MIPAV's application, making it a versatile tool for researchers across various biomedical disciplines. The ability to handle diverse datasets underscores MIPAV's relevance in the broader context of life sciences and biomedical research.

Looking forward, ambitious goals for MIPAV include leveraging Java's distributed execution capabilities to enhance algorithm performance. This strategic direction aligns with advancements in distributed computing and cloud-based solutions. By harnessing the distributed computing capabilities of Java, MIPAV aims to improve the scalability and efficiency of its algorithms, enabling faster and more robust processing of large datasets. This forward-looking approach ensures that MIPAV remains at the forefront of innovation in medical image processing.

In conclusion, the ongoing development of MIPAV underscores a commitment to excellence in medical image processing and analysis. By expanding functionalities, embracing advanced techniques, and adapting to the diverse needs of the NIH user community, MIPAV continues to be a versatile and valuable tool in the realm of biomedical research. The incorporation of cutting-edge features, such as volume rendering, advanced segmentation, and distributed computing capabilities, positions MIPAV as a dynamic and forward-thinking platform that will contribute significantly to advancements in medical imaging and research.

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