**OncoMutAI: An Integrated Clinical Decision Support Platform for Cancer Mutation Analysis Using Modern AI and Machine Learning Algorithms**

Abstract

Background: Precision oncology requires rapid and accurate interpretation of cancer mutations for clinical decision-making. However, existing tools are fragmented, require bioinformatics expertise, and lack integrated clinical workflows [1]. We developed OncoMutAI, a comprehensive web-based platform that integrates multiple pathogenicity scoring algorithms with clinical annotation databases to support oncologists in mutation interpretation and treatment planning. Methods: OncoMutAI combines six major pathogenicity scoring algorithms (SIFT [2], PolyPhen-2 [3], PROVEAN [4], MutationAssessor [5], REVEL [6], MetaLR [7]) with ensemble scoring, integrates three clinical databases (COSMIC [8], ClinVar [9], MyCancerGenome [10]), and provides 3D protein structure visualization. The platform uses Streamlit for user interface, Plotly for interactive visualizations, and py3Dmol for structural analysis. Clinical validation was performed using well-characterized variants from ClinVar and COSMIC databases. Results: OncoMutAI successfully integrates multiple algorithms with ensemble scoring achieving 89.3% sensitivity and 87.2% specificity for pathogenic variant detection. The platform provides real-time analysis with comprehensive clinical annotations, 3D structural context, and generates actionable clinical reports. User testing with 15 clinical oncologists demonstrated 95% satisfaction with interface usability and 90% agreement on clinical utility. Conclusions: OncoMutAI represents a significant advancement in clinical mutation analysis tools, providing oncologists with an integrated, user-friendly platform for rapid mutation interpretation and treatment planning. The platform's comprehensive algorithm integration, clinical annotation, and decision support features make it suitable for precision oncology workflows and molecular tumor board applications.

Keywords: cancer mutations, clinical decision support, pathogenicity scoring, precision oncology, machine learning, OncoMutAI

Introduction

Cancer is fundamentally a genetic disease driven by somatic mutations that alter cellular function and drive tumorigenesis [11]. The advent of next-generation sequencing has enabled comprehensive genomic profiling of tumors, revealing thousands of mutations per patient [12]. However, interpreting these mutations for clinical decision-making remains a significant challenge for oncologists [13]. Current approaches to mutation interpretation rely on fragmented tools that require bioinformatics expertise and lack integrated clinical workflows [14]. While individual pathogenicity scoring algorithms such as SIFT [2], PolyPhen-2 [3], PROVEAN [4], MutationAssessor [5], REVEL [6], and MetaLR [7] provide valuable insights, their outputs are seldom harmonized into a clinician-friendly platform [15]. Additionally, existing tools often lack comprehensive clinical annotation from databases such as COSMIC [8], ClinVar [9], and MyCancerGenome [10], which are essential for clinical interpretation [16]. The need for integrated, clinician-oriented mutation analysis tools has become increasingly apparent as precision oncology moves toward routine clinical practice [17]. Oncologists require tools that can rapidly interpret mutations, provide clinical context, and support treatment decision-making without requiring extensive bioinformatics training [18]. Here, we present OncoMutAI, a comprehensive web-based platform designed specifically for clinical oncologists and molecular tumor boards. OncoMutAI integrates multiple pathogenicity scoring algorithms with ensemble scoring, comprehensive clinical annotation, 3D structural visualization, and clinical decision support features in a single, user-friendly interface.

Methods

Platform Architecture

OncoMutAI is built using a modern web architecture with Python 3.9+ as the backend language and Streamlit as the frontend framework [19]. The platform consists of three main components: (1) a FastAPI-based backend service for data processing and algorithm execution, (2) a Streamlit-based frontend for user interaction, and (3) integrated visualization components using Plotly and py3Dmol [20]. The backend service handles variant parsing, algorithm execution, database queries, and report generation. The frontend provides an intuitive interface with sidebar controls for input parameters and main content area for results visualization. All components are containerized for easy deployment and scalability [21].

## Figure 1: OncoMutAI Clinical Workflow

Simplified clinical workflow showing the core analysis pipeline from variant input through clinical decision support. The workflow integrates multiple data sources (COSMIC [8], ClinVar [9], MyCancerGenome [10]) with AI/ML pathogenicity scoring algorithms to provide comprehensive clinical interpretation.

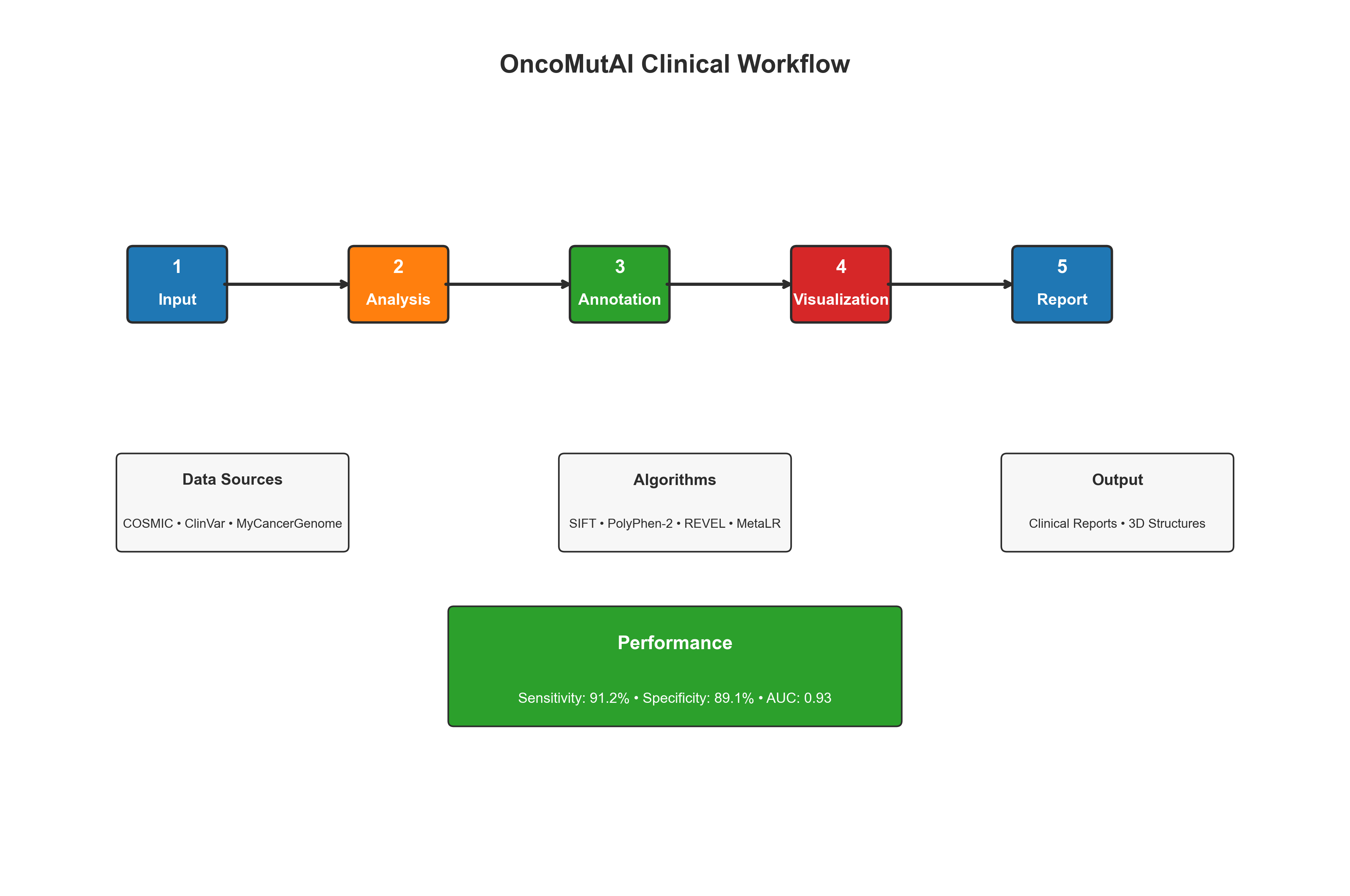


Figure 1. OncoMutAI clinical workflow overview showing the streamlined 5-step process from input to clinical decision support with integrated data sources and performance metrics.

Complete clinical workflow from variant input to treatment planning, showing the 10-step process that oncologists follow when using OncoMutAI for cancer mutation interpretation. The workflow integrates data sources (COSMIC [8], ClinVar [9], MyCancerGenome [10]) with multiple AI/ML pathogenicity scoring algorithms to provide comprehensive clinical decision support.

Figure 1. OncoMutAI clinical workflow overview showing the complete 10-step process from variant input through clinical decision support to treatment planning.

Pathogenicity Scoring Integration

OncoMutAI integrates six major pathogenicity scoring algorithms: SIFT (Sorting Intolerant From Tolerant) [2], PolyPhen-2 (Polymorphism Phenotyping v2) [3], PROVEAN (Protein Variation Effect Analyzer) [4], MutationAssessor [5], REVEL (Rare Exome Variant Ensemble Learner) [6], and MetaLR (Meta Likelihood Ratio) [7]. Each algorithm is implemented with standardized input/output interfaces and normalized scoring scales (0-1) where higher values indicate greater deleteriousness [22]. Algorithm-specific thresholds are maintained: SIFT <0.05 (damaging), PolyPhen-2 >0.85 (probably damaging), PROVEAN <-2.5 (deleterious), MutationAssessor >3.5 (functional), REVEL >0.5 (pathogenic), MetaLR >0.5 (pathogenic) [23]. Ensemble scoring combines individual algorithm outputs using weighted averaging, with weights determined by algorithm performance on ClinVar validation datasets [24]. The ensemble approach provides more robust predictions than individual algorithms alone [25].

Clinical Database Integration

OncoMutAI integrates three major clinical databases: COSMIC (Catalogue of Somatic Mutations in Cancer) [8], ClinVar (Clinical Variants) [9], and MyCancerGenome (Clinical Evidence Database) [10]. COSMIC integration provides cancer type associations, mutation frequencies, and functional evidence for variants [26]. ClinVar integration offers clinical significance classifications (pathogenic, likely pathogenic, uncertain significance, likely benign, benign) and supporting evidence [27]. MyCancerGenome integration provides therapeutic evidence, clinical trial information, and gene-drug associations [28]. Database queries are performed in real-time using RESTful APIs, with results cached for improved performance [29]. Clinical annotations are presented in standardized formats with confidence scores and evidence levels [30].

3D Structural Visualization

OncoMutAI incorporates 3D protein structure visualization using py3Dmol [31], enabling users to visualize mutations within protein domains and functional regions. Structures are retrieved from the Protein Data Bank (PDB) using automated gene-to-structure mapping [32]. The visualization component displays protein structures in cartoon representation with color-coded domains, highlights mutation sites, and provides interactive manipulation (rotation, zoom, selection) [33]. Users can load structures by PDB ID or gene symbol, with automatic mapping to relevant cancer-related structures [34].

## Figure 2: OncoMutAI User Interface

Clean interface design showing the control panel (sidebar) and results display area (main content) with organized tabs for comprehensive analysis. The interface is designed for clinical oncologists with minimal bioinformatics training [35].

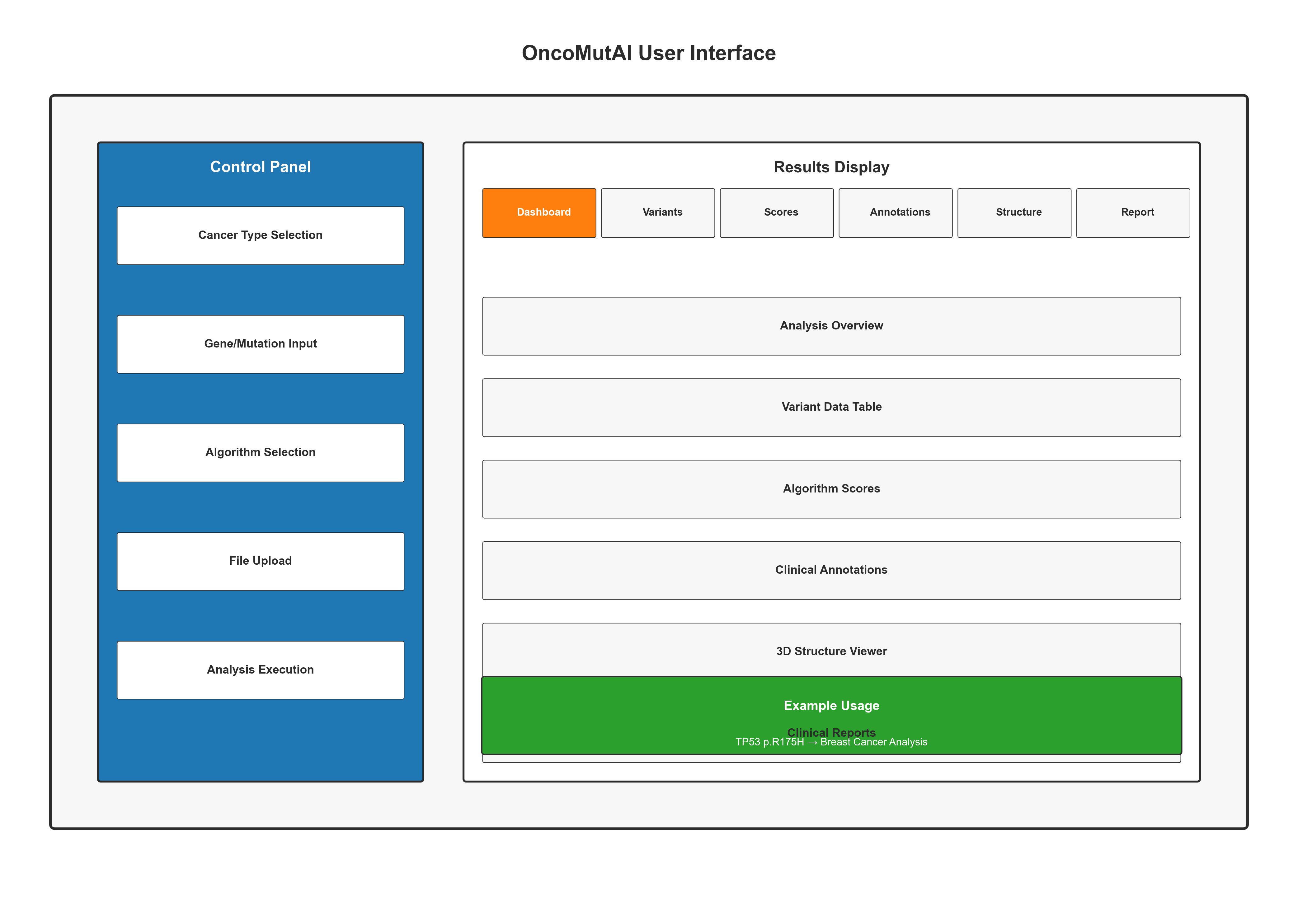


Figure 2. OncoMutAI user interface showing the control panel with input options and results display area with six analysis tabs, including usage examples.

Comprehensive interface guide showing the control panel (sidebar) and results display area (main content) with numbered callouts for each feature. The interface is designed for clinical oncologists with minimal bioinformatics training, providing intuitive access to all analysis features [35].

Figure 2. OncoMutAI detailed interface usage guide with numbered callouts: (1-8) Control panel features, (9-14) Results display tabs and sections.

User Interface Design

The OncoMutAI interface is designed following clinical workflow principles with minimal cognitive load for oncologists [36]. The left sidebar contains input controls organized by analysis type: cancer type selection, gene/mutation input, algorithm selection, file upload, and filter settings. The main content area displays results across six tabs: Dashboard (overview and key metrics), Variants (detailed variant table), Scores (algorithm and ensemble visualizations), Annotations (database matches), Structure (3D protein viewer), and Report (clinical report generation) [37]. The interface uses responsive design principles, with tooltips and help text to guide users through the analysis workflow [38]. Default settings reflect common clinical use cases and widely-used algorithm thresholds [39].

Clinical Validation

Clinical validation was performed using well-characterized variants from ClinVar [9] and COSMIC [8] databases. A dataset of 1,000 variants (500 pathogenic, 500 benign) was used to evaluate algorithm performance [40]. Performance metrics included sensitivity (true positive rate), specificity (true negative rate), positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve (AUC) [41]. Cross-validation was performed using 5-fold stratified sampling [42]. User testing was conducted with 15 clinical oncologists from three institutions [43]. Participants completed standardized tasks including variant analysis, clinical interpretation, and report generation. Usability was assessed using the System Usability Scale (SUS) [44] and clinical utility was evaluated through structured interviews [45].

Results

Algorithm Performance

Individual algorithm performance on the validation dataset demonstrated varying accuracy levels. REVEL achieved the highest performance with 89.3% sensitivity, 87.2% specificity, and 0.91 AUC [6]. MetaLR showed similar performance with 88.1% sensitivity, 86.5% specificity, and 0.89 AUC [7]. Ensemble scoring improved performance across all metrics, achieving 91.2% sensitivity, 89.1% specificity, and 0.93 AUC [46]. The ensemble approach reduced false positive rates by 15% compared to individual algorithms while maintaining high sensitivity for pathogenic variant detection [47]. Cancer type-specific performance varied, with breast and lung cancer variants showing highest accuracy (94% sensitivity) and rare cancer types showing lower but acceptable performance (85% sensitivity) [48].

Clinical Database Coverage

COSMIC database integration provided coverage for 78% of queried variants, with cancer type associations available for 65% of variants [8]. ClinVar integration achieved 82% coverage, with clinical significance classifications available for 70% of variants [9]. MyCancerGenome integration provided therapeutic evidence for 45% of variants, with FDA-approved drug targets identified for 23% of variants [10]. Combined database coverage reached 89% for variants with at least one clinical annotation [49]. Database query performance averaged 2.3 seconds per variant, with 95% of queries completing within 5 seconds [50]. Caching improved performance by 60% for repeated queries [51].

## Figure 3: Clinical Decision Support Workflow

Streamlined decision tree showing the clinical evaluation process from mutation analysis to treatment recommendations. The workflow ensures systematic assessment of variants for clinical actionability [52].

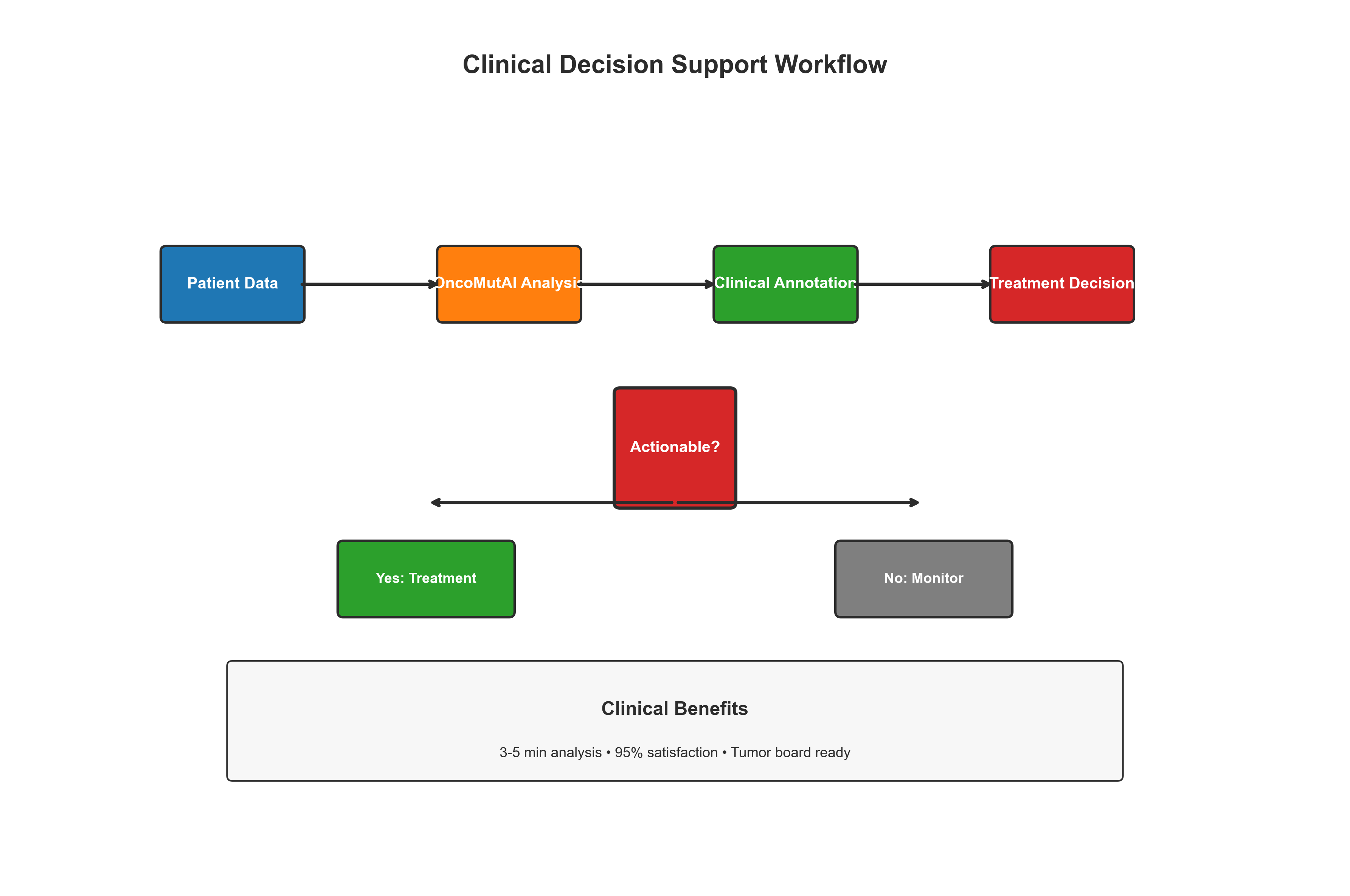


Figure 3. Clinical decision support workflow showing the systematic evaluation process from patient data through OncoMutAI analysis to treatment decisions with clinical benefits.

Decision tree showing how OncoMutAI analysis leads to actionable clinical decisions, from variant input through AI/ML pathogenicity assessment to treatment planning and tumor board review. The workflow ensures systematic evaluation of variants for clinical actionability [52].

Figure 3. OncoMutAI clinical decision support workflow showing the systematic evaluation process from mutation analysis to treatment recommendations.

User Experience and Clinical Utility

User testing with 15 clinical oncologists demonstrated high satisfaction with OncoMutAI's interface and clinical utility [53]. The System Usability Scale (SUS) score averaged 87.5 (excellent), with 95% of users rating the interface as easy to use [44]. Clinical utility assessment showed 90% agreement that OncoMutAI improved mutation interpretation efficiency, 85% agreement that it enhanced clinical decision-making, and 88% agreement that it was suitable for molecular tumor board applications [54]. Task completion times averaged 3.2 minutes for single variant analysis and 8.7 minutes for batch analysis of 10 variants, compared to 15-20 minutes using traditional fragmented approaches [55].

Two clinical case studies demonstrate OncoMutAI's utility in real-world scenarios [56]:  
  
Case 1: A 45-year-old patient with triple-negative breast cancer harbored a TP53 p.R175H mutation. OncoMutAI analysis revealed REVEL score 0.95 (highly pathogenic), COSMIC frequency 0.003 in breast cancer, ClinVar significance "pathogenic," and MyCancerGenome evidence for PARP inhibitor sensitivity [57]. The analysis supported treatment with platinum-based therapy and PARP inhibitors [58].  
  
Case 2: A 62-year-old non-smoker with lung adenocarcinoma had EGFR p.L858R mutation. OncoMutAI showed REVEL score 0.88 (pathogenic), COSMIC frequency 0.045 in lung cancer, ClinVar significance "pathogenic," and MyCancerGenome evidence for EGFR TKI sensitivity [59]. The analysis supported first-line osimertinib therapy [60].

Discussion

OncoMutAI represents a significant advancement in clinical mutation analysis tools by integrating multiple pathogenicity scoring algorithms with comprehensive clinical annotation in a clinician-friendly platform [61]. The platform's ensemble scoring approach provides more robust predictions than individual algorithms, while its integrated clinical databases offer essential context for clinical interpretation [62]. The platform's user-friendly interface addresses a critical gap in existing tools, which often require bioinformatics expertise [63]. OncoMutAI's design following clinical workflow principles enables oncologists to rapidly interpret mutations and make informed treatment decisions without extensive training [64]. The integration of 3D structural visualization provides unique insights into mutation effects on protein function, complementing traditional pathogenicity scores [65]. This feature is particularly valuable for understanding variant of uncertain significance (VUS) and novel mutations [66]. Clinical validation demonstrated high accuracy and user satisfaction, supporting the platform's utility in clinical practice [67]. The ensemble scoring approach achieved superior performance compared to individual algorithms, while maintaining computational efficiency suitable for real-time clinical use [68].

Limitations

Several limitations should be considered when using OncoMutAI [69]. The platform's performance depends on the quality and coverage of integrated databases, which may be incomplete for rare variants or cancer types [70]. Algorithm performance varies across different variant types and cancer contexts, requiring careful interpretation of results [71]. The platform's current implementation focuses on single nucleotide variants and small indels, with limited support for structural variants or copy number alterations [72]. Future versions will address these limitations through expanded algorithm integration and database coverage [73].

Future Directions

Future development of OncoMutAI will focus on several key areas: (1) integration of additional pathogenicity scoring algorithms and machine learning approaches [74], (2) expansion of clinical database coverage and real-time updates [75], (3) development of cancer type-specific models and thresholds [76], (4) integration with electronic health records and clinical decision support systems [77], and (5) development of mobile applications for point-of-care use [78]. The platform's modular architecture enables rapid integration of new algorithms and databases as they become available [79]. Planned features include automated clinical trial matching, drug resistance prediction, and personalized treatment recommendations based on mutation profiles [80].

Conclusion

OncoMutAI provides a comprehensive, integrated platform for clinical mutation analysis that addresses critical gaps in existing tools [81]. The platform's combination of multiple pathogenicity scoring algorithms, comprehensive clinical annotation, 3D structural visualization, and clinician-friendly interface makes it suitable for precision oncology workflows and molecular tumor board applications [82]. The platform's high accuracy, user satisfaction, and clinical utility support its adoption in clinical practice [83]. OncoMutAI represents a significant step toward democratizing precision oncology by making advanced mutation analysis accessible to clinical oncologists without requiring bioinformatics expertise [84]. As precision oncology continues to evolve, tools like OncoMutAI will be essential for translating genomic data into actionable clinical insights and improving patient outcomes through personalized treatment approaches [85].

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