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## A Review on CASA-Computer-Assisted Semen Analysis

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### Abstract

Computer-Assisted Semen Analysis (CASA) has emerged as a revolutionary tool in reproductive medicine, offering objective, accurate, and repeatable assessment of sperm parameters that were traditionally evaluated manually and subjectively. This review provides a comprehensive overview of the development, principles, applications, and technological advancements of CASA systems. It highlights how CASA has improved the evaluation of sperm motility, concentration, morphology, and other kinematic parameters in both human and animal semen. Additionally, the paper explores recent innovations including AI integration, microfluidics, and smartphone-based analysis, while discussing the limitations of current systems, such as sensitivity to sample preparation and lack of standardization. The review also identifies future research directions aimed at enhancing diagnostic precision and accessibility in andrology and fertility science. Overall, CASA continues to evolve as a critical technology in the pursuit of improving reproductive health outcomes.

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## Introduction

The assessment of semen quality is a cornerstone of male fertility evaluation in both human and veterinary medicine. Traditionally, this process has relied on manual examination under a microscope to assess parameters such as sperm count, motility, and morphology. However, manual semen analysis is often labor-intensive, time-consuming, and prone to significant subjectivity and inter-observer variability (World Health Organization, 2021; Amann and Waberski, 2014; Mortimer, 2000; Versteegen *et al.*, 2002). In response to these challenges, Computer-Assisted Semen Analysis (CASA) systems were developed to provide a more objective, standardized, and reproducible method for evaluating semen samples (Yániz *et al.*, 2015; Kwon *et al.*, 2015; Gao *et al.*, 2020; Martínez *et al.*, 2017).

Since their introduction in the late 20th century, CASA systems have transformed the landscape of reproductive diagnostics by automating the measurement of sperm kinematics and morphology using digital imaging and sophisticated software algorithms (Su *et al.*, 2013; Cheng *et al.*, 2020; Moghaddam and Borji, 2011; Zhou *et al.*, 2021). These systems are capable of analyzing thousands of spermatozoa in a matter of seconds, yielding quantitative data on motility characteristics (such as velocity, trajectory, and progression), concentration, and structural integrity.

CASA has become a vital tool not only in clinical andrology labs but also in animal breeding, toxicology, cryopreservation research, and assisted reproductive technologies (ART) (Blanchard *et al.*, 2011; Filimberti *et*

*al.*, 2013). Despite their widespread adoption, CASA systems are not without limitations (Jung and Cho, 2019; Agarwal *et al.*, 2019; Dearing *et al.*, 2014; Dearing *et al.*, 2021). Challenges remain in areas such as standardization across platforms, accurate identification of sperm cells in heterogeneous samples, and adaptability to different species or clinical contexts (Singh *et al.*, 2011; Knuth and Nieschlag, 1988).

With the emergence of advanced technologies—including artificial intelligence, machine learning, and microfluidic integration—CASA is poised for a new era of innovation.

This review aims to explore the historical development, core components, practical applications, current limitations, and future prospects of CASA technology.

Through this analysis, the review seeks to provide a comprehensive understanding of CASA's role in modern reproductive science and its potential to further enhance fertility diagnostics and treatment outcomes.

## Principles and Components of CASA

CASA systems are designed to quantitatively assess sperm parameters using digital imaging, automated tracking, and statistical analysis. The typical components of a CASA system include:

- **Microscope with camera:** Captures video or still images of semen samples.
- **Image acquisition and processing software:** Detects and tracks sperm cells frame-by-frame.
- **Analytical algorithms:** Calculate motility, morphology, concentration, and kinematic parameters.
- **Data output and visualization tools:** Provide tabulated results and graphical representations.

Key sperm parameters evaluated by CASA include:

- **Motility:** Percentage of motile vs. immotile sperm; progressive vs. non-progressive movement.
- **Velocity parameters:**
  - VCL (Curvilinear Velocity)
  - VSL (Straight-Line Velocity)
  - VAP (Average Path Velocity)
- **Linearity and amplitude** of sperm movement.
- **Morphology:** Head size/shape, midpiece integrity, and tail abnormalities.
- **Concentration and viability.**

## Applications of CASA

### Clinical Andrology

CASA is widely used in fertility clinics for routine semen evaluation, sperm selection for intrauterine insemination (IUI), in vitro fertilization (IVF), and monitoring treatment outcomes (Brito *et al.*, 2016; Komori *et al.*, 2006; Jędrzejczak *et al.*, 2005; Freour *et al.*, 2009; Auger *et al.*, 2016).

### Veterinary Medicine

In livestock breeding and conservation programs, CASA supports semen quality assessments in species like bulls, boars, stallions, dogs, and endangered animals.

### Reproductive Toxicology

CASA is valuable for assessing the effects of environmental toxins, pharmaceuticals, and radiation on sperm function, offering standardized quantification for toxicological studies.

### Research and Cryopreservation

It plays a key role in reproductive biology research and evaluating the efficacy of cryopreservation protocols by quantifying post-thaw sperm viability and motility.

## Advantages of CASA

- **Objectivity:** Eliminates human bias in sperm evaluation.
- **Speed and Throughput:** Analyzes thousands of sperm in seconds.
- **Reproducibility:** Produces consistent results across tests and users.
- **Detailed Kinematic Analysis:** Tracks individual sperm trajectories and movement patterns.
- **Quantitative Morphometry:** Provides exact measurements of sperm dimensions.

## Limitations and Challenges

Despite its advantages, CASA faces several limitations:

- **Sensitivity to Sample Preparation:** Semen dilution, debris, or poor slide preparation can affect accuracy.
- **Species-Specific Calibration:** Algorithms need adaptation for different animal species.

- **Standardization Issues:** Lack of global standards in threshold values and parameter definitions.
- **Software Variability:** Different CASA systems may yield inconsistent results due to proprietary algorithms.

## Recent Technological Advances

### Artificial Intelligence and Machine Learning

AI-enhanced CASA systems improve sperm recognition, reduce false tracking, and enable advanced classifications of motility patterns and morphological anomalies.

### Smartphone-Based CASA Systems

Portable, low-cost CASA solutions using smartphone cameras and optical attachments are emerging for point-of-care and at-home semen analysis.

### Microfluidics Integration

Microfluidic platforms combined with CASA can simulate physiological environments, allowing for functional sperm sorting based on chemotaxis or thermotaxis.

### Cloud and Remote Diagnostics

Cloud-connected CASA tools allow clinicians to analyze data remotely, enabling decentralized fertility diagnostics and global data-sharing for research.

### Standardization Efforts

Efforts are underway to harmonize CASA standards, particularly through:

- **WHO Laboratory Manual for Semen Analysis (6th Edition, 2021).**
- **International Society of Andrology (ISA) guidelines.**
- **Development of open-source CASA frameworks** to improve accessibility and transparency.

### Future Directions

The future of CASA is expected to include:

- **Multimodal Sperm Profiling:** Combining CASA with genomic, proteomic, and epigenetic data.

- **Real-Time, In Vivo Analysis:** Studying sperm dynamics within reproductive tracts using advanced imaging.
- **Personalized Fertility Monitoring:** Using mobile CASA tools integrated with health apps.
- **Cross-Species AI Models:** Unified CASA platforms adaptable for human and veterinary use.
- **Open-Source Platforms:** Reducing costs and expanding research access in low-resource settings.

## Conclusion

Computer-Assisted Semen Analysis (CASA) has revolutionized the field of reproductive science by providing an objective, consistent, and high-throughput method for evaluating sperm quality. From clinical fertility assessments to animal breeding and reproductive research, CASA systems have significantly improved the accuracy and reliability of semen analysis compared to traditional manual methods. Despite their wide applicability, current CASA technologies face limitations, including sensitivity to sample conditions, species-specific adaptability, and lack of global standardization. However, ongoing advancements in artificial intelligence, smartphone integration, microfluidics, and open-source development are rapidly enhancing the precision, accessibility, and functionality of these systems. As CASA continues to evolve, it is expected to play an increasingly vital role in personalized reproductive health, remote diagnostics, and fertility research. With cross-disciplinary collaboration and continued technological innovation, CASA will remain a key pillar in advancing both human and veterinary andrology in the years to come.

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