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Review Article

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Automation in Intracytoplasmic Sperm Injection: Technologies, Outcomes, and Future Directions

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Abstract

Since 1992, intracytoplasmic sperm injection (ICSI) has become an important technique in assisted reproduction. In male-factor infertility, fertilization is enabled by the microsurgical insertion of a single sperm cell directly into the cytoplasm of an oocyte. The majority of in vitro fertilization cycles worldwide employ ICSI, which is performed manually by trained embryologists. However, automation is being pursued to improve overall uniformity and efficiency, because manual ICSI is labor-intensive and subject to variability that depends on the skill of the embryologist. This article outlines the state of the art in ICSI automation, including computer vision-guided control mechanisms, robotic micromanipulation systems, and artificial intelligence (AI) for sperm selection. It discusses the technical advances that enable robots to perform key ICSI steps with high precision, such as automated sperm detection, sperm capture, oocyte detection, oocyte fixation, and injection using microneedles and piezoelectric actuators. Emerging AI algorithms that evaluate and select optimal sperm in real time, as well as machine learning-based imaging systems for oocyte and embryo assessment, are also examined. Current outcomes from studies of automated ICSI are presented, including the first healthy births achieved with a robotic ICSI platform, and technical and clinical results are compared with those of conventional manual ICSI. Finally, future directions and challenges are explored, such as the integration of multiple laboratory procedures into an autonomous workflow, as well as safety, regulatory, and ethical considerations. Automation in ICSI has begun to show considerable promise for advancing reproductive technology, heralding a new era of innovation in embryology laboratories.

Keywords:
intracytoplasmic sperm injection; in vitro fertilization; assisted reproductive technology; automation; robotics; artificial intelligence; computer vision

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1. Introduction

The development of intracytoplasmic sperm injection (ICSI) in the early 1990s revolutionized the treatment of male-factor infertility. In 1992, Palermo and colleagues achieved the first successful human pregnancies through ICSI [1]. Since then, ICSI has been rapidly adopted worldwide and, by 2013, was used in approximately 70% of all in vitro fertilization (IVF) cycles [2]. This widespread utilization exceeds the proportion of infertility cases strictly attributable to male-factor causes, reflecting an expansion of ICSI beyond its original indication [3,4]. Large-scale studies in the United States have shown that ICSI offers no significant improvement in outcomes for couples without male-factor infertility compared with conventional IVF [4].

Nevertheless, the technique's popularity has continued to grow, contributing to an estimated several million births globally through ICSI [5].

Manual ICSI is a technically demanding microsurgical procedure. It is typically performed using an inverted microscope equipped with micromanipulators and involves immobilizing a single sperm and injecting it through the oolemma into the oocyte's cytoplasm using a fine glass pipette [1] (Figure 1). The outcome of ICSI

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is highly operator-dependent; subtle differences in technique can affect fertilization and embryo development [6,7]. For example, the site of sperm deposition and the method of oolemma penetration may influence oocyte survival and fertilization rates [7,8]. Greater cytoplasmic aspiration has been associated with reduced blastocyst development, although no differences were observed in the chromosomal endpoints assessed [9]. To minimize such risks, embryologists orient the oocyte's internal structures prior to injection (often by rotating the oocyte so that the first polar body is at the 6 or 12 o'clock position) to avoid the meiotic spindle [10]. The success of the ICSI procedure therefore depends on a high degree of microsurgical skill and experience. Operator expertise has been correlated with fertilization rates and blastocyst development; experienced practitioners achieve consistently higher success rates, whereas trainees show greater variability [6,11]. In one analysis, embryos derived from ICSI performed by highly experienced embryologists had significantly higher sustained implantation rates than those from less experienced operators [6]. ICSI is also labor-intensive, requiring a single embryologist to inject oocytes sequentially. A typical ICSI cycle may involve dozens of oocytes, and prolonged exposure of oocytes outside the incubator during the injection process can be detrimental [12,13]. Pujol et al. reported that a longer retrieval-to-ICSI interval was associated with lower biochemical and clinical pregnancy rates [13]. Furthermore, the delicate nature of ICSI raises certain safety considerations. For instance, historical comparisons of assisted reproduction with spontaneous conception raise safety concerns, although the available evidence does not distinguish the contribution of ICSI from that of IVF [14].

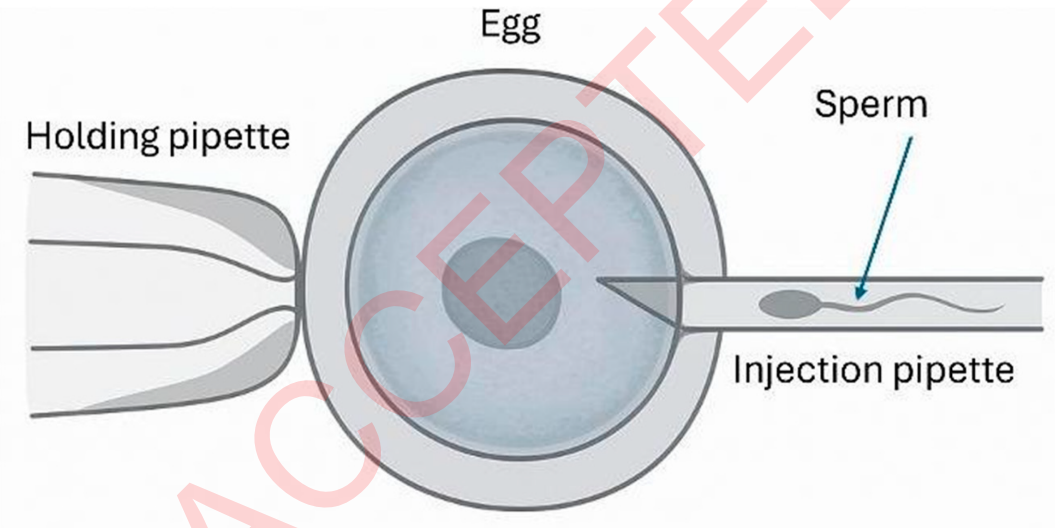

Figure 1: Intracytoplasmic sperm injection (ICSI).

Given the high technical demands, inter-operator variability, and throughput limitations of manual ICSI, there has been considerable interest in automating the ICSI process. Automation offers the potential to standardize technique, reduce human error, and reduce the workload in IVF laboratories [15,16]. In recent years, researchers have begun to apply advanced technologies, including precision robotics, microfluidic devices, artificial intelligence (AI), and computer vision, to replicate the actions of an embryologist during ICSI. Initial milestones have already been achieved, including the first reported births from robot-assisted ICSI in 2023 [17].

International experts have begun to establish best-practice guidelines and performance indicators for IVF laboratory operations (e.g., the Vienna consensus for assisted reproductive technology (ART) laboratories) [18], and automated systems will be required to meet or exceed these quality benchmarks. With continued innovation, ICSI automation may augment the work of human embryologists and help to make IVF more consistent, accessible, and efficient for the growing number of patients worldwide seeking assisted reproduction [19].

This review provides an overview of the current state of automation in ICSI. It first summarizes the conventional manual ICSI procedure and its limitations. It then examines the emerging technologies that enable ICSI automation: robotic micromanipulation systems, AI-driven sperm selection methods, and computer vision coupled

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with intelligent control software (e.g., the ROS2 robotics framework). Subsequently, it compares the technical performance and early clinical outcomes of automated ICSI with those of manual practice. Finally, it discusses future directions, including the integration of additional laboratory steps into automated platforms, and considers the remaining technical, regulatory, and ethical challenges on the path toward fully automated IVF. Figure 2 summarizes the major milestones in ICSI automation development.

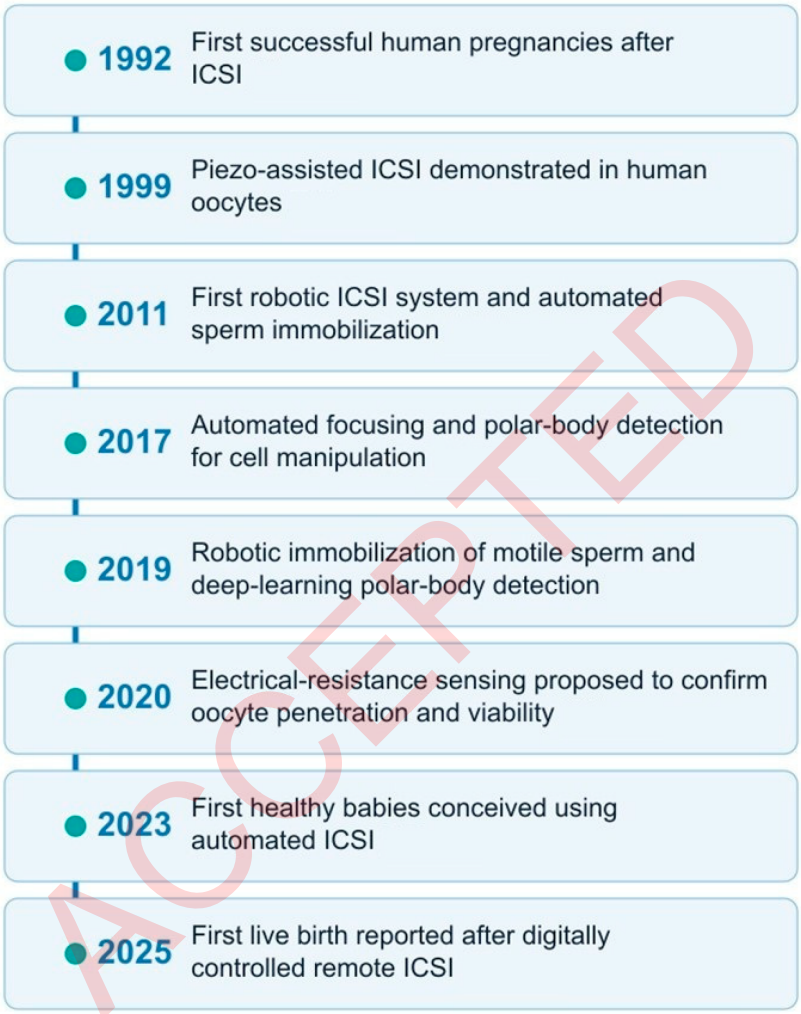

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Figure 2: Major milestones in ICSI automation. Dates reflect publication or reported clinical achievement, and reference numbers correspond to the manuscript bibliography.

2. Manual ICSI Overview

In the standard ICSI procedure, a single spermatozoon is injected directly into the cytoplasm of a mature oocyte using micromanipulation under microscopic guidance [1]. The oocyte is held in place by a holding pipette, while an injection pipette (approximately 5–6 μm inner diameter) is used to penetrate the zona pellucida and oolemma and deposit the sperm. Before injection, sperm are typically immobilized (by tail scoring) to facilitate aspiration into the needle. The embryologist then advances the injection pipette into the oocyte, usually entering at the 3 o'clock position to avoid the meiotic spindle apparatus located near the polar body [10]. Gentle suction is then applied to aspirate a small amount of ooplasm along with the sperm, followed by expulsion of the sperm into the oocyte. Fertilization rates of approximately 70% can be achieved by skilled operators, who minimize cytoplasmic leakage through precise pipette withdrawal.

Subtle differences in technique influence success rates, as ICSI demands a high level of skill. Nagy et al. demonstrated that both the sperm deposition site and the

oolemma rupture technique (abrupt vs. slow penetration) affect fertilization and embryo development [7]. Palermo et al. reported a correlation between post-ICSI oocyte survival and certain oolemma features, such as pliability, indicating varying vulnerability to injection-induced damage [8]. Consequently, improper pipette placement or excessive force during insertion may lead to aberrant oocyte activation or permanent damage [9]. Therefore, before injection, embryologists meticulously position the oocyte and frequently employ instruments such as polarized light microscopy to verify the spindle location [10]. Evidence indicates that an embryo is less likely to develop normally when the spindle is misaligned relative to the injection angle [10].

ICSI is a technically challenging procedure; thus, the operator performing it has a substantial impact on success rates. Tiegs and Scott reported that, whereas less experienced personnel had higher rates of complete fertilization failure, experienced embryologists achieved substantially higher rates of fertilization and blastocyst formation [6]. In a high-volume IVF center, maintaining consistent results across staff members can be difficult. Moreover, manual ICSI is difficult to scale. Only one oocyte can be injected at a time by an embryologist, and each oocyte requires several minutes. Processing a batch of fifteen to twenty oocytes can easily take more than an hour. During this time, the oocytes remain outside the incubator and are exposed to ambient conditions, which may induce cellular stress. Pujol et al. demonstrated that longer intervals between oocyte retrieval and sperm injection reduced fertilization and pregnancy rates [13]. Performing this procedure manually for hours is also physically demanding for embryologists. During lengthy laboratory sessions, such fatigue can readily lead to minor losses of precision [11,12]. ICSI carries slightly higher risks than standard IVF, including a modest increase in de novo chromosomal abnormalities or birth defects, although the procedure is generally safe [14]. This may result from the physically invasive nature of ICSI and its circumvention of natural sperm selection. Although these risks are small, they constitute a major reason why researchers seek to refine and standardize the technique.

Over the years, incremental refinements have been made to the manual ICSI process to improve success rates and reduce oocyte trauma. One major innovation was the use of piezoelectric actuators to facilitate oocyte membrane penetration. Initially demonstrated in animals such as mice [20] and later applied to humans [21,22], piezo-ICSI involves mounting the injection pipette onto a device that delivers rapid mechanical pulses. These piezo pulses drive the pipette through the zona and oolemma with minimal deformation of the oocyte, reducing the force required by the operator. Yanagida et al. reported in 1999 that a piezo microinjector could improve fertilization and embryo development in humans, particularly in cases of hardened zona pellucida [21]. Zander-Fox et al. demonstrated that piezo-ICSI increases fertilization rates compared with standard ICSI, particularly in patients older than 38 years [23,24]. In a clinical comparison, Takeuchi et al. reported improved fertilization and cleavage with piezo-assisted zona penetration followed by conventional oolemma puncture [22]. Piezo actuation has become routine for ICSI in certain animal species (e.g., mouse ICSI), where it markedly increases the survival of oocytes that are otherwise highly sensitive to mechanical stress [20]. Other technological advances include specialized pipette designs. For instance, Fernandez et al. developed a modified holding pipette that prevents the loss of essential cellular material during injection by holding the oocyte steady without aspirating excess cytoplasm [25]. Additionally, researchers have investigated the incorporation of haptic feedback into micromanipulators. This helps the embryologist avoid applying excessive force to the oocyte by enabling the operator to perceive the resistance against the pipette [26]. Collectively, these technological advances have substantially improved the reliability of manual ICSI. Nevertheless, the process remains highly complex and depends entirely on the embryologist's expertise. To minimize human error and improve consistency, researchers are currently investigating automation. Regardless of who operates the equipment, consistently high fertilization rates might be achieved by automating the precise movements and decisions involved in sperm injection. Automation might also expedite the procedure, thereby reducing cellular stress and oocyte handling times.

3. Automation Technologies

3.1. Robotics and Micromanipulation Systems

At the heart of ICSI automation is robotic technology, which aims to precisely and consistently reproduce the delicate actions of an embryologist. Early work in this area began more than a decade ago. In 2011, Lu et al. reported a robotic ICSI system that used computer-controlled actuators and visual tracking to guide sperm injection [27]. Leung and colleagues independently developed an automated sperm-immobilization apparatus that visually tracked a motile sperm and controlled a micropipette to immobilize it, achieving an 88.2% immobilization success rate in 1000 trials [28]. Building on these advances, Zhang et al. demonstrated a clinically oriented robotic platform that achieved 96.0% sperm-head track-

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ing success and 94.5% immobilization success across 400 sperm, distinguishing tracking performance from the immobilization outcome [29]. Collectively, these studies established that key ICSI subtasks can be automated reproducibly.

Modern robotic ICSI workstations typically consist of high-precision mechanical micromanipulators (sometimes piezo-actuated) mounted on an inverted microscope, all under computer control. These systems can execute the same steps as a human operator: capture a sperm cell, position the injection needle, puncture the oocyte, and inject the sperm. Electrical resistance measurement has also been proposed as a method for confirming oolemma penetration and oocyte viability during manual or robotic ICSI [30]. Costa-Borges et al. reported normal fertilization in 13 of 14 robot-injected donor oocytes and the birth of two healthy babies after transfer of robot-derived euploid blastocysts [17]. This marked the first reported instance of live human births from robot-performed sperm injections. Shortly thereafter, a case report described the first baby born from a remotely operated ICSI procedure, in which an operator in one location controlled a robot in an IVF laboratory at another site to carry out the sperm injection. Most of the ICSI micromanipulation steps in that system were automated, with the remainder executed by the robot under remote human guidance [31]. This system is a partially automated, remotely controlled ICSI platform built entirely from commercially available components. It comprises an inverted microscope with a heated stage, a laser for non-contact cutting, a piezo actuator, a motorized XY stage, a motorized objective turret, oil/air microinjectors, and high-resolution cameras. Together, these components enable the entire ICSI process to be monitored and controlled digitally (Figure 3).

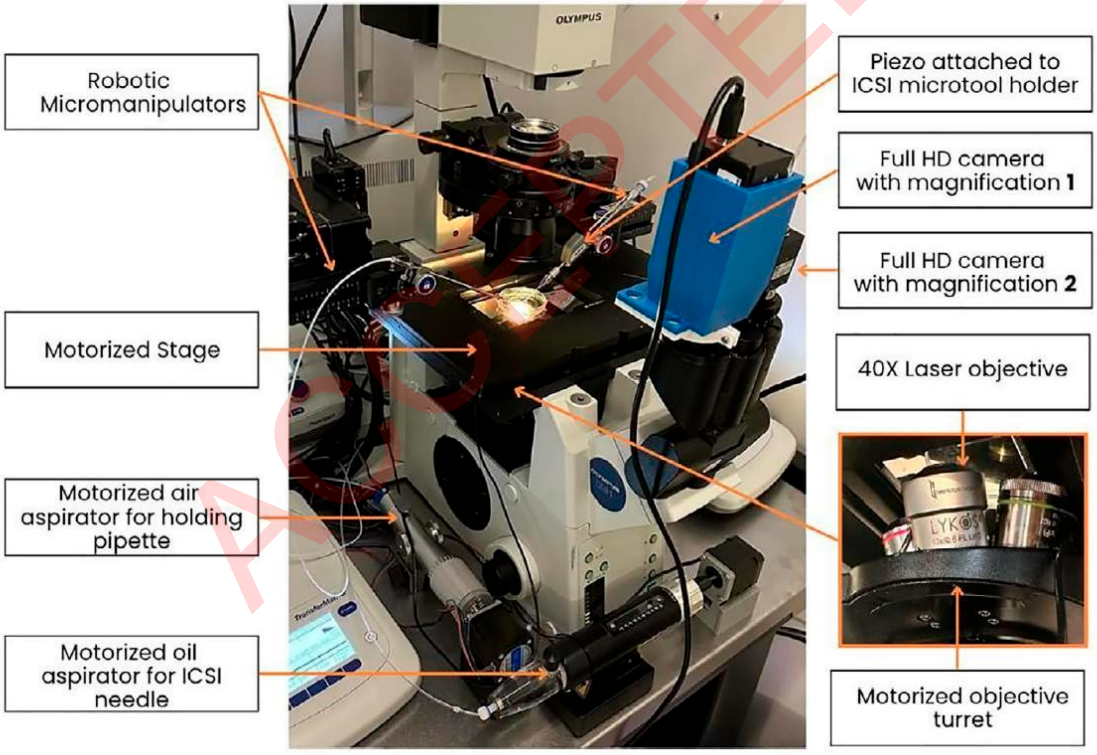

Figure 3: The remotely controlled and motorized intracytoplasmic sperm injection experimental setup. Reproduced from Mendizabal-Ruiz et al. [31] under CC BY-NC-ND license.

These milestone achievements underscore the potential of robotics to reproduce the delicate maneuvers of ICSI. Notably, the robotic system developed by Costa-Borges et al. employs a piezoelectric drill on the injection pipette that is triggered automatically by the control software to penetrate the oocyte membrane, rather than relying on the tactile judgment of an embryologist [17]. This ensures the consistent application of the minimum necessary force. The same system automates critical steps such as precise pipette positioning and depth control, under the oversight of computer vision and AI algorithms. Beyond sperm injection itself, robotics is being introduced into other laboratory tasks associated with ICSI. For example, robotic systems have been developed to automate the

preparation of embryo culture dishes and the handling of microdroplets for IVF, tasks traditionally performed manually. Lattin et al. (2024) described an automated robotic platform for preparing embryo culture dishes with consistent medium droplets and oil overlay, improving standardization in the IVF laboratory [32]. There are also efforts to robotically automate oocyte handling before and after ICSI, for instance, transferring oocytes from one dish to another or loading them into a microfluidic device. Ultimately, fully automated IVF workstations may integrate several functions, including sperm sorting, ICSI, embryo culture, and cryopreservation. Palermo and colleagues have patented a design for a microfluidic-based "ICSI device" that combines all steps of sperm injection into a single closed system. Their design includes reservoirs and channels for holding oocytes, loading sperm, and culturing embryos. This design effectively consolidates several pieces of laboratory equipment into a single disposable microfluidic chip [33]. If developed at a larger scale, this system might reduce laboratory costs while also minimizing the risks of contamination, human error, and manual labor. However, realizing this goal will require the integration of precise robotics, reliable microfluidics, and stringent environmental controls.

Robotic ICSI relies on sophisticated control software that uses sensor data to coordinate motors and actuators in real time. For this type of laboratory and medical robotics, the Robot Operating System 2 (ROS2) is frequently employed [34]. In addition to allowing real-time operation and feedback loops, ROS2 provides a flexible, modular architecture that facilitates the connection of various devices, such as micromanipulators, cameras, and piezo actuators. Unlike previous ROS versions, ROS2 was designed to meet the real-time, safety, and reliability requirements of critical systems. It employs a data distribution service (DDS) that can be configured for deterministic, low-latency communication between components. In optimized setups, sub-millisecond timing of actions is achievable, though this depends on the specific DDS implementation, transport, and system tuning rather than being a default guarantee. In ICSI automation, a ROS2-based control system can simultaneously manage the motion of the injection pipette, the holding pipette, the microscope stage, and any auxiliary devices (e.g., a piezo driver or laser), while receiving continuous updates from imaging systems. Park et al. (2020) demonstrated ROS2's capability for multi-agent real-time coordination, which is directly applicable to controlling multiple robotic axes in an ICSI procedure [35]. While Mendizabal-Ruiz et al. [31] described a digitally controlled remote ICSI system using proprietary software interfaces without explicitly naming the underlying framework, such teleoperated platforms typically rely on ROS-like middleware design patterns to ensure low-latency command translation [31]. Reliable control is critical; for example, to instantly halt injection if unexpected resistance is detected, or to execute a series of piezo pulses with precise timing and amplitude. As robotic ICSI systems evolve, their control software will increasingly incorporate sophisticated decision-making algorithms (such as AI-driven adjustments based on live imaging), but ROS2 provides the backbone to integrate these higher-level functions with the low-level motor control safely and in real time [35].

In summary, robotic micromanipulation systems have advanced from the proof-of-concept devices of the early 2000s to current clinically tested prototypes. As demonstrated by fertilization and blastocyst rates comparable to those of manual ICSI in early studies, these systems can automate the mechanical aspects of ICSI with high precision. Although the number of cases remains very small, robotic ICSI has already resulted in healthy births [17,31]. At present, these systems still require human supervision or a hybrid configuration in which an engineer may remotely supervise certain components while other processes operate automatically [31]. However, clinics are progressing toward complete autonomy as the technology becomes established. Robotics and intelligent software can take over the repetitive, physically demanding aspects of ICSI, allowing embryologists to concentrate solely on supervision and critical decisions. A fully automated laboratory process is becoming increasingly attainable as this type of automation extends to other areas of the IVF facility. Strict IVF safety standards must be upheld as this technology is implemented, and each automated stage must handle oocytes and sperm with the same care as a skilled embryologist. Early results are encouraging, and ongoing refinements (such as better force feedback, more sensitive vision systems, and improved microfabricated devices for handling gametes) will further enhance robotic ICSI performance.

3.2. AI-Assisted Sperm Selection

Selecting a viable, high-quality spermatozoon is a prerequisite for successful ICSI. In conventional practice, an embryologist subjectively selects a sperm cell by assessing its morphology (e.g., head shape, absence of vacuoles) and motility under magnification. This process is inherently variable and dependent on the operator's judgment and experience. In recent years, artificial intelligence has been introduced to assist in and standardize sperm selection for ICSI [15,16]. AI-driven sperm selection tools typically use computer vision and machine learning algorithms to evaluate sperm images or videos in real time and identify

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the sperm cell most likely to result in successful fertilization and development.

A representative example of such a tool is the Sperm Selection Diagnoscope (SiD) software developed by Mendizabal-Ruiz et al. [36]. SiD employs a form of artificial vision and machine learning to analyze the motility patterns of individual sperm in real time during an ICSI procedure. In a study of 383 sperm videos, this AI system computed quantitative motility parameters such as straight-line velocity and head-movement periodicity and generated a "score" for each sperm based on features that correlated with successful fertilization and blastocyst formation. The authors found that sperm selected by embryologists that subsequently fertilized oocytes and formed blastocysts had significantly higher AI-derived scores (indicating more linear and less erratic movement) than those that failed [36]. These findings suggest that AI can detect subtle differences in sperm behavior that are predictive of fertilization success. This retrospective analysis illustrates the potential of quantitative motility features to support sperm assessment, although prospective studies are required to determine their value for selection and clinical outcomes.

Artificial intelligence has shown promise in assisting with sperm assessment and selection. In a systematic review of 34 studies published between 2010 and 2023, Cherouveim et al. identified applications involving sperm morphology, motility, and DNA integrity. The authors concluded that AI could improve the objectivity and reproducibility of sperm assessment but emphasized that model performance depends heavily on the size and quality of the training dataset [15].

Automated sperm selection extends beyond basic digital imaging. Other novel methods are also being integrated into automated workflows. Microfluidic sperm sorting devices, for instance, offer a means of selecting sperm based on physical and fluid-dynamic properties (such as motility and the ability to navigate microchannels) without manual pipetting. These chips can be regarded as a form of "passive" automation for sperm selection. Recent clinical data indicate that microfluidic sperm selection can improve ICSI outcomes in certain scenarios. The chip-selected sperm also yielded a greater number of high-quality embryos, suggesting that this method enriched for physiologically competent sperm [37]. Automated systems can incorporate such microfluidic modules to perform sperm selection upstream of the ICSI robot. For example, an integrated platform might use a microfluidic device to isolate the most suitable sperm, then an AI-enabled microscope to select the optimal sperm from among them, and finally a robot to inject it, thereby combining physical and AI-based selection mechanisms. Such developments indicate that future automated ICSI workstations will likely include a sperm selection subsystem where sperm are processed and evaluated by AI prior to injection.

Integrating AI into sperm selection aims to make the process more objective and data-driven. By continuously learning from large datasets of sperm features and ICSI outcomes, AI systems could potentially identify sperm characteristics (or combinations of characteristics) that are not readily apparent to human observers. AI can identify minute irregularities in sperm head movement or subtle morphological defects associated with DNA damage that human observers might overlook. By ensuring that the injected sperm has the highest possible chance of producing a viable embryo, the use of these methods could readily improve ICSI success or embryo quality. AI may reduce the uncertainty and subjective bias that typically led to inconsistent outcomes by standardizing selection across different personnel and laboratories, even if it only establishes a baseline. Nevertheless, before widespread adoption, these AI tools still require rigorous validation. Although they can score or rank sperm, the ultimate proof of efficacy lies in improved clinical outcomes (fertilization, embryo development, live birth rates) in controlled studies. To date, limited data (mostly from retrospective analyses) suggest equivalent or improved outcomes with AI-assisted selection [36], although additional prospective trials are needed.

Overall, AI-assisted sperm selection is a rapidly evolving component of ICSI automation. It complements mechanical robotics by addressing the decision-making aspect of gamete selection. In an automated ICSI scenario, a sperm cell could be automatically isolated on a microfluidic platform, after which an AI system would evaluate it alongside others to select the top candidate, and finally a robot would inject the chosen sperm into the oocyte. Each of these steps (isolation, evaluation, and injection) can be integrated for seamless operation. Currently, many clinics are beginning to adopt AI systems in a decision-support role (with the embryologist still making the final decision), but fully automated selection is on the horizon. As these technologies continue to advance, the practice of an embryologist peering into a microscope to subjectively select a sperm cell may give way to an era in which intelligent machines identify the "best" sperm for injection based on measurable criteria and big-data insights. Figure 4 summarizes the integrated, closed-loop workflow from sperm selection through post-injection verification.

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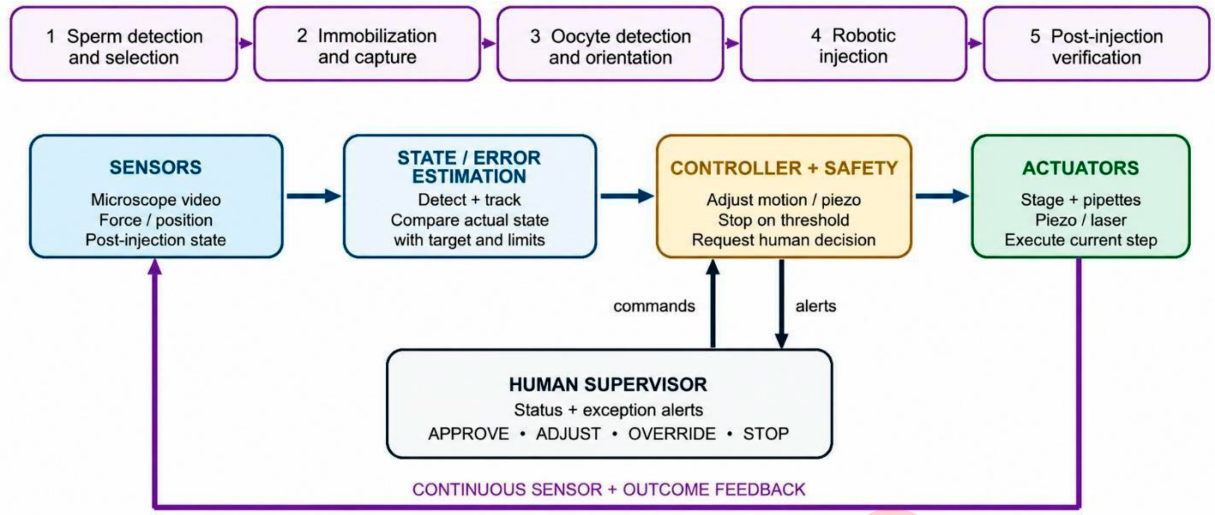

Figure 4: Human-supervised closed-loop control for automated ICSI. Sensor measurements are converted into a state/error estimate, the controller updates robotic motion and actuation, and the measured result is fed back continuously. The operator receives status updates and exception alerts and may approve, adjust, override, or stop the procedure.

3.3. Computer Vision and Robotic Control

Automating ICSI would not be possible without sophisticated computer vision to replicate the visual function of the embryologist and advanced control software to coordinate movements based on visual feedback. High-resolution imaging and real-time image analysis (often facilitated by AI algorithms) enable a robot to "see" and respond during the delicate steps of ICSI. One of the fundamental tasks is the identification and localization of the oocyte and key structures (such as the polar body) in the dish. Conventional ICSI relies on the embryologist's visual assessment to orient the oocyte correctly. In an automated system, computer vision algorithms assume this role. Researchers have developed methods to automatically detect oocytes and their orientation using image processing techniques. Chen et al. (2016) described an algorithm capable of recognizing the outline of an oocyte and the presence of the polar body in microscope images using contour detection and machine learning classification (support vector machines) [38]. In subsequent work, Wang et al. (2019) implemented a deep learning approach for polar body detection that remained robust even under varying illumination or slight differences in oocyte shape (Figure 5) [39]. These algorithms allow the robotic control system to determine the location of the polar body so that the injection pipette can be directed to the opposite side, avoiding damage to the spindle. Similarly, computer vision can track the injection needle's position and angle relative to the oocyte. Wang et al. (2017) demonstrated an autofocus and image-detection system that keeps both the oocyte and injection pipette in sharp focus and can detect the pipette tip's position relative to the oocyte's membrane [16]. This ensures that the robot advances the needle the correct distance into the oocyte before releasing the sperm.

Another critical aspect of future closed-loop control is monitoring oolemma behavior. Yagi et al. retrospectively analyzed recordings from 93 oocytes, including 38 with rupture and 55 without rupture, and investigated rupture prediction using image features and a support vector machine [40]. This was a rupture-prediction study and did not demonstrate real-time automatic termination of piezo pulses. Prospective integration would require the validation of decision thresholds, latency, and effects on oocyte survival.

To handle such real-time decisions, the control software, often built on frameworks such as ROS2, must integrate visual data with actuator control. The robot's control algorithm continuously processes the live video feed: when the oocyte is in view, it calculates the target coordinates for injection based on the oocyte's geometry; as the pipette moves, it adjusts course if the pipette drifts from the target or if the oocyte moves; when the pipette tip contacts the oolemma, it triggers the piezo driver and watches for the membrane break; once detected, it halts further movement and commands sperm release. All of these actions occur on the order of milliseconds to seconds. ROS2's real-time messaging and multi-threaded handling enable parallel processing of these tasks (one thread for image analysis, one for motion control, etc.) without compromising synchronization [35]. In essence, computer vision provides the feedback loop that turns open-

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loop robotic motion into a closed-loop controlled process, much as an embryologist continuously adjusts hand movements by watching through the eyepiece. Researchers have also sought full 3D visualization of oocytes and microneedles to guide robots more accurately. Tang et al. (2021) reviewed approaches for achieving automated rotation and orientation of biological cells in micromanipulation [41]. Techniques such as microvortex flows and optical traps can reorient oocytes or embryos, and 3D machine vision can be employed to identify an oocyte's spatial orientation from multiple angles [41]. Although not yet routine in ICSI, these methods could eventually allow a robot to automatically rotate an oocyte to the desired orientation (for example, turning the oocyte until the polar body is detected at the top) without human intervention, before performing the injection. This would be especially useful in a fully enclosed microfluidic system where manual rotation via a holding pipette may be challenging.

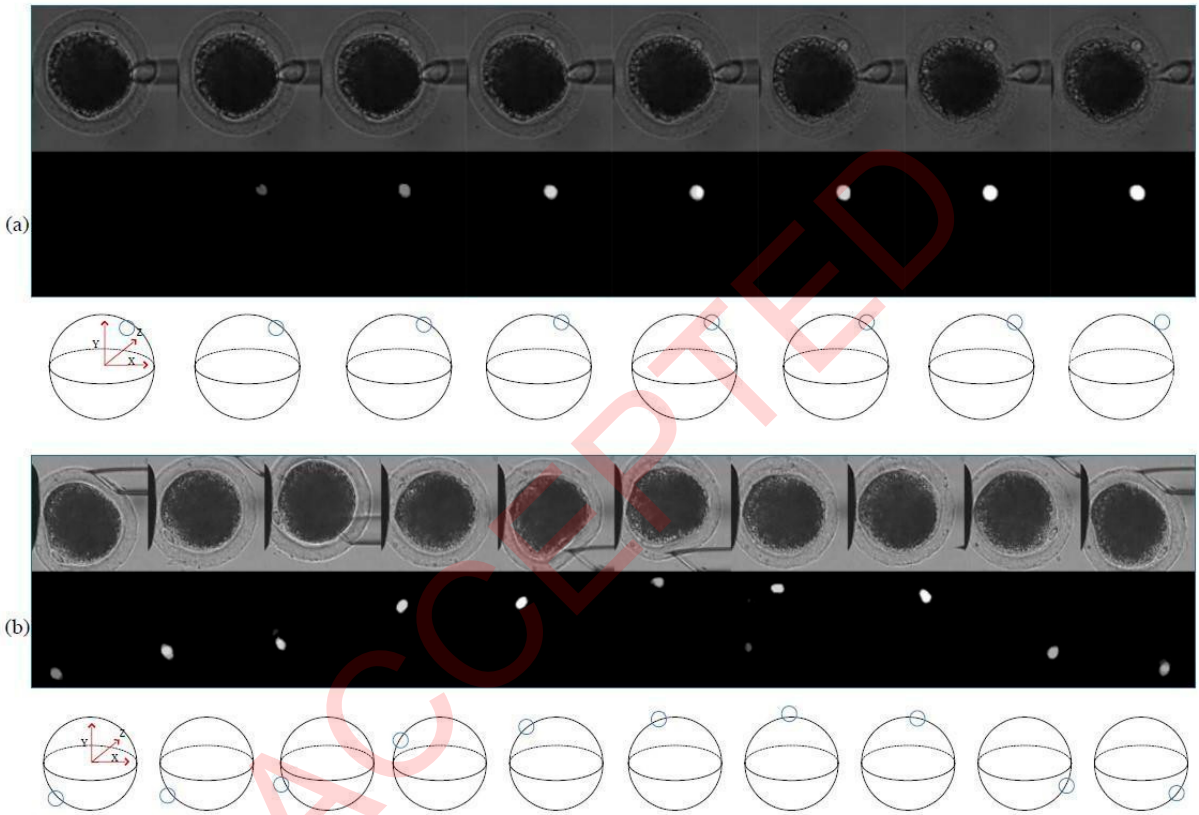

Figure 5: Polar body detection results for two oocytes. (**a**) Different visibilities. (**b**) Different rotations. Reproduced from Wang et al. [39] under CC BY license.

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Another sensor modality that can complement vision is force sensing, which measures the resistance on the injection pipette. Some automated systems incorporate miniature force sensors or measure pressure changes to detect when the pipette has penetrated the zona and oolemma. Johnson et al. (2018) introduced a flexure-guided piezo drill that reduced lateral vibration and deformation during zona penetration in mouse oocytes [42]. In a robotic context, force feedback can work in parallel with vision: the vision system guides the pipette to the oocyte, and the force sensor confirms penetration and can prevent overshooting the far side of the oocyte. Ensuring that the robot exerts only the minimum necessary force is essential for oocyte viability.

Recent studies have also explored lightweight computer vision approaches for sperm detection in microdissection testicular sperm extraction (micro-TESE) procedures. One such system, SD-CLIP (Sperm Detection using Classical Image Processing), was designed for sperm-scarce environments associated with non-obstructive azoospermia (NOA) [43]. Unlike computationally intensive deep-learning pipelines, SD-CLIP employs morphology-based image processing and principal component analysis to identify sperm heads and tails in unstained differential interference contrast (DIC) mi-

croscopy images. The method achieved substantially reduced computational time and lower false-positive rates than previous MB-LBP-based approaches, while maintaining practical clinical applicability for real-time sperm retrieval support [43]. The authors also suggested integrating such lightweight systems into future automated sperm extraction and robotic ART platforms [43]. Beyond standalone detection systems, researchers have also begun to integrate AI-based analysis directly into microscope visualization workflows. Augmented reality (AR) systems combined with AI-based computer vision are also emerging as promising tools for assisted reproductive procedures. Mohamed et al. proposed an AI-assisted AR microscope system for Micro-TESE that integrates YOLOv5-based sperm detection, DeepSORT tracking, and real-time visual overlays within the microscope eyepiece [44]. Figure 6 illustrates the overall concept of the AR-assisted microscope system and its real-time visualization workflow. The system provides immediate visual guidance to embryologists by highlighting detected sperm and displaying motility-related information during microscopic examination. Compared with previous handcrafted methods, operator testing revealed a sperm-detection rate of 66.9% with AR versus 30.8% without AR, an approximately 2.17-fold increase, or a 36.1-percentage-point difference [44]. This configuration demonstrates how integrating AI with augmented reality might accelerate the sperm search process in the laboratory by reducing the embryologist's physical and visual strain.

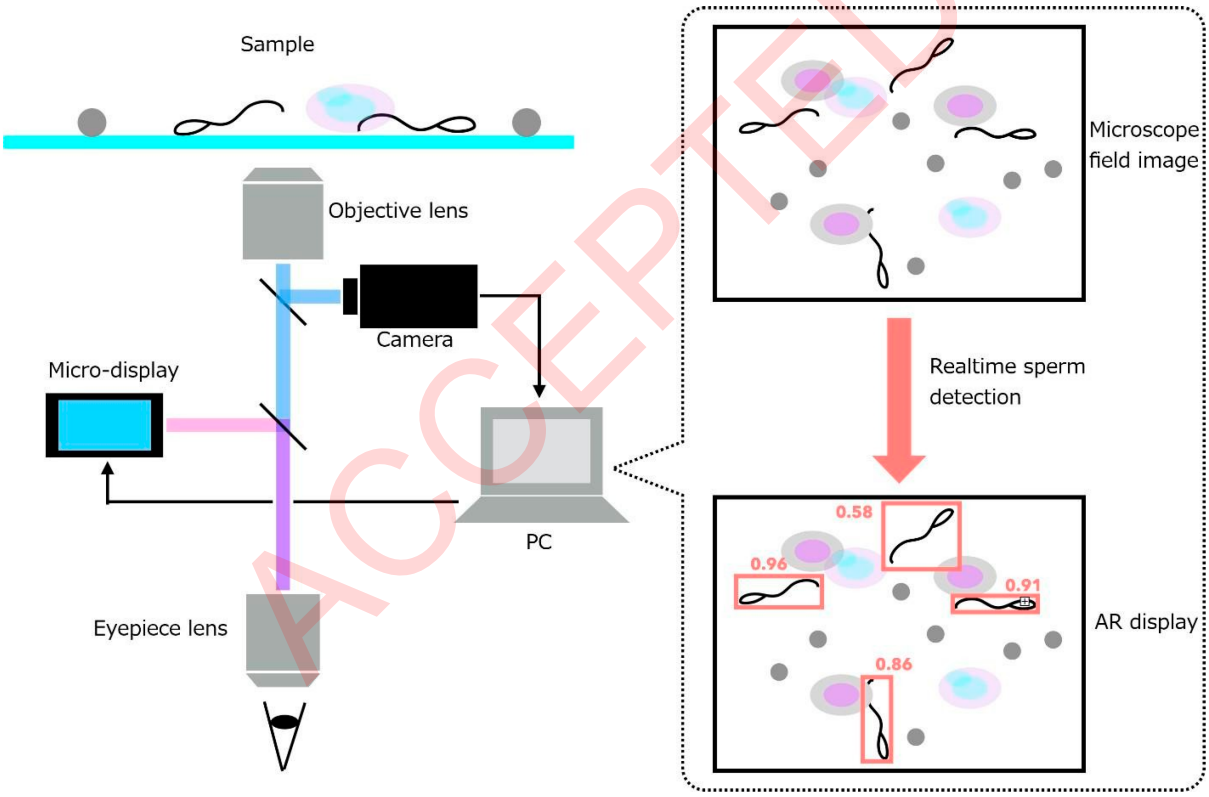

Figure 6: Conceptual overview of the AI-assisted augmented-reality microscope system for real-time sperm detection and tracking during Micro-TESE procedures. Adapted from Mohamed et al. [44] under CC BY license.

In brief, the fundamental building blocks of automated ICSI are computer vision and intelligent software. They manage both the sensory input and the actual decision-making, enabling the robot to monitor visual changes and modify its actions instantaneously. To date, researchers have successfully automated the focusing and alignment of injection instruments [16], as well as the detection of oocytes and polar bodies [38,39]. Current systems can identify sperm in intricate Micro-TESE environments using lightweight models [43], predict oolemma rupture from images [40], and employ augmented reality powered by AI to assist with sperm retrieval [44]. Together, these advances improve consistency in individual automation tasks, although clinical equivalence to expe-

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rienced embryologists remains to be established. Vision software will likely incorporate more sophisticated AI features in the future. Rather than merely monitoring the polar body, advanced algorithms might assess oocyte maturity or identify vacuoles associated with poor oocyte quality, instantly adjusting the injection parameters.

The system can respond to dynamic laboratory conditions by integrating computer vision with control architectures such as ROS2. When a sperm or oocyte moves within the pipette, the robot recognizes the change and immediately adjusts its trajectory. Although automated ICSI systems currently rely on simple image processing, precision will continue to be driven by technological advances. For instance, spectral imaging could assess cell health during handling, and increasing frame rates and resolutions will enhance the detection of the "zona pellucida rupture" at the precise instant of puncture. A gentle, reliable, and highly repeatable process is ensured by controlling these inputs within a real-time control loop. A smooth, delicate, and repeatable injection process will be achieved by feeding all of these data streams into the control loop managed by ROS2 or comparable architectures.

3.4. Technical and Clinical Outcomes

The ability of any automated ICSI approach to match or surpass the results achieved by proficient human practitioners constitutes the ultimate test. Fertilization rate (percentage of injected oocytes that fertilize normally), embryo development rate (e.g., blastocyst formation rate), embryo quality, live birth rate, and offspring health are key outcome indicators. Multiple healthy blastocysts and euploid embryos were obtained, suggesting that automated injection may not have compromised oocyte and embryo viability. In the 2023 study, normal fertilization occurred in 13 of 14 robot-injected and 16 of 18 manually injected donor oocytes, and two singleton births followed transfer of robot-derived euploid blastocysts [17]. These findings provide early evidence of clinical feasibility and support larger comparative studies. Mendizabal-Ruiz et al. similarly reported a successful live birth from their digitally controlled, remote ICSI system, a case that underscores the potential for teleoperated or fully automated fertilization in settings where experienced embryologists may not be physically present [31].

From a technical standpoint, these initial applications of automated ICSI have highlighted both achievements and areas for improvement. On the positive side, the consistency of the robotic movements can reduce some forms of oocyte trauma. The ICSIA system, for example, applies highly standardized piezo pulse patterns for membrane penetration, which may avoid excessive oolemma stretching or cytoplasmic turbulence that can occur with variable manual force [17]. Additionally, a robot does not fatigue or lose focus, and each injection is performed with the same steady hand. This could be particularly beneficial in cases with high oocyte yield (e.g., certain patients with polycystic ovary syndrome), in which an embryologist might inject dozens of oocytes in a single session. It is conceivable that automation could maintain high performance even after numerous injections, whereas a human operator might become more prone to errors or slower over time.

On the other hand, current automated systems still have certain technical limitations, which are reflected in the clinical results. One limitation is sperm selection and loading, which in reported cases was still performed manually. This means that overall success still depended partly on the human factor of selecting a suitable sperm. If that selection was suboptimal, the outcomes (failed fertilization or poor embryo development) would not necessarily be attributable to the robot. Going forward, the incorporation of AI-based sperm selection could further improve outcomes by systematically picking sperm with higher developmental potential (e.g., those with high motility and low DNA fragmentation). Another observed challenge is that the robotic system needs to accommodate variability in oocyte properties (size, zona thickness, etc.). Human operators intuitively adjust injection dynamics for a very large oocyte or a very thick zona (for instance, by applying more piezo pulses). A robot might initially use a uniform approach. If an oocyte requires slightly more force and the robot's preset is too gentle, it could fail to penetrate on the first attempt, necessitating multiple attempts that might stress the oocyte. Conversely, if it is too aggressive for a given oocyte, it might cause an avoidable fracture in the zona. Fine-tuning adaptive control, perhaps using force feedback or computer vision cues, will be needed to handle such variability. For instance, one group is investigating algorithms to predict whether an oocyte is at risk of rupture from injection and modulate the approach accordingly [40].

In terms of embryo development and clinical pregnancy rates, larger studies will be required to determine whether automated ICSI can match the gold standard set by expert embryologists. The two live births achieved through the automated system resulted in healthy infants with normal birth weights [17], suggesting the technique does not disrupt early development. However, randomized controlled trials are required to demonstrate therapeutic efficacy. Future studies should employ a split-oocyte design, dividing a patient's oocytes between robotic and manual injection to directly compare embryo progression and outcomes. Given the ethical and practical hurdles,

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more observational data may first accumulate from cases where automation is used out of necessity or in validation studies.

Beyond fertilization metrics, other technical outcomes of interest include procedure time and throughput. One goal of automation is to increase efficiency. In the remote ICSI case report, the authors noted that approximately 50% of the steps (e.g., fine positioning, injection actuation) were performed autonomously, which helped to standardize the procedure [31]. The total time per injection was reported to be similar to that of an experienced operator, though not necessarily faster [31]. With further optimization, robots could potentially perform injections faster or in parallel (for example, a multi-pipette system injecting multiple oocytes simultaneously, if engineered). Even modest time savings per oocyte can translate into oocytes spending less time in suboptimal conditions, potentially improving outcomes for sensitive oocytes (such as those from older patients). Another technical outcome is the error rate, that is, how often the robot misses or drops an oocyte or fails to inject properly. In manual ICSI, it is not uncommon for an oocyte to lyse if mishandled or for the spindle to be aspirated accidentally. An automated system should achieve an error rate no worse (and ideally better) than the human benchmark. To date, reports of automated cases have not described any catastrophic errors, although the numbers remain small. Developing robust error-detection mechanisms (such as recognizing whether the sperm was not actually deposited and repeating the attempt) remains an ongoing area of research.

One noteworthy consideration is whether automation could enable improvements in environments or conditions that are challenging for humans. For example, microgravity in space makes manual ICSI nearly impossible owing to the lack of sedimentation and handling difficulties, but a robotic system could potentially operate in a closed chamber in space with minor modifications. Chaplia et al. argued that, as humans contemplate reproduction beyond Earth, automated systems will be essential to perform delicate ART procedures in non-terrestrial environments [45]. Although purely theoretical at this stage, this possibility suggests that automated ICSI might have unique advantages in specialized scenarios (extreme environments, remote locations with telemedicine, etc.) that extend beyond simply replacing an embryologist in a standard clinic.

In animal reproduction and research, automated microinjection has already yielded notable outcomes. Robotic microinjection systems have been used to inject large batches of zebrafish embryos for research, achieving very high survival and hatching rates [46,47]. Wang et al. developed a fully automated system for zebrafish embryo microinjection (not sperm injection, but transgene injection) that could process embryos in an assembly-line manner with a success rate of around 99% [46]. Although fish embryos differ considerably from human oocytes, these successes in other models underscore how automation can drastically improve throughput without sacrificing viability. Similarly, a force-sensing multi-cell injection robot was able to inject dozens of fish embryos with consistent quality, a task that would be extremely tedious for a human to perform individually [48]. The outcomes (in terms of embryo survival to hatching) were comparable to those achieved by manual experts, but with much higher speed [48]. These research analogues suggest that automated ICSI could maintain high performance over large numbers of oocytes, which might be beneficial in animals such as livestock where dozens of oocytes are routinely handled, or in humans if IVF ever moves toward mild stimulation with many small cohorts across multiple sessions.

In human clinical use, an automated ICSI system will ultimately be judged by live birth rates and neonatal health outcomes. The initial case reports are reassuring, but long-term follow-up of a larger number of children will be required. Notably, even manual ICSI remains the subject of ongoing debate regarding subtle risks (as mentioned, slightly higher de novo genetic abnormalities or epigenetic concerns have been raised [14]). Developers must ensure that automation does not introduce additional mechanical stress or alter handling times in ways that impact imprinting. To date, no such complications have been reported. Furthermore, standard IVF safety protocols, such as preimplantation genetic testing and detailed prenatal screening, are well equipped to detect any early genetic or developmental abnormalities.

Overall, small clinical studies suggest that automated ICSI matches the success rates and feasibility of conventional manual methods. Robotic systems have achieved high fertilization rates, high blastocyst development, and successful pregnancies. Although these results are preliminary, they provide a proof of principle that automation need not compromise effectiveness. As larger datasets are accumulated, it will become clear whether automation can consistently match the fertilization and live birth per egg retrieval statistics that are common with manual ICSI in good-prognosis patients. There is reason to be optimistic that it can, given the precise control and lack of fatigue in robots. Moreover, automation could excel in scenarios where manual performance might decline, for example, during very lengthy procedures or with very difficult samples (e.g., an extremely low motile sperm count, in which AI might help identify the single viable sperm). The ultimate measure of success will be widespread clinical adoption, which will only occur if outcomes under

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automation are at least as good as those achieved by top embryologists. The coming years will likely see iterative improvements to address the current limitations (such as fully automating sperm loading and refining vision algorithms), leading to even more reliable performance. With these advances, it would be reasonable to expect automated ICSI results to match or even outperform manual results in certain areas, for example, by almost completely preventing oocyte lysis or continuously increasing fertilization even under unfavorable circumstances. Until then, the collaborative model (human oversight with robotic assistance) might serve as a bridge that delivers favorable results while fostering confidence in the technology.

4. Future Directions and Challenges

Several significant prospects and challenges lie ahead as automation in ICSI and IVF continues to progress. The complete automation of the fertilization process will be one of the main priorities. Current robotic ICSI systems perform the mechanical injection effectively but still rely on humans for upstream and downstream steps such as sperm processing, oocyte handling, and embryo culture. In the future, these could be integrated into a single seamless automated workflow. For example, an oocyte could be picked up from a retrieval dish by a robotic arm, loaded into a microfluidic ICSI chip, automatically injected with a sperm, then moved into an onboard culture chamber, all without human contact. Achieving this will require the integration of multiple modules: sperm selection, injection, and embryo culture. Some progress is already evident. Patents have been filed for comprehensive IVF platforms that incorporate sperm preparation and ICSI in one system [33,49]. Millan et al. have developed a robotic system for sperm preparation that uses AI to automate steps such as mixing, centrifugation, and aspiration of the semen sample [50]. The same group also patented an automated vitrification device for oocytes/embryos, where a robot can carry out the delicate series of transfers into cryoprotectant solutions and onto a cryo-device with minimal manual input [51]. In the coming years, these components, such as automated sperm preparation, automated ICSI, and automated embryo handling, can be expected to become interconnected, leading to the first truly "closed" IVF systems. Such closed systems would enhance reproducibility and potentially reduce the risk of human error (for instance, eliminating the chance of sample misidentification or mishandling between steps). They could also improve laboratory safety by minimizing exposure of gametes to the external environment.

Despite this encouraging trajectory, many obstacles must still be overcome before fully automated IVF becomes commonplace. Ensuring the reliability and safety of automated systems is a major challenge. Because every oocyte and embryo is valuable, reproductive medicine has an extremely low tolerance for error. Robotic systems require robust error-detection and recovery mechanisms to be fail-safe. For example, instead of injecting air or harming the oocyte, a robotic ICSI system should identify the problem and either retry or notify a human operator if it is unable to pick up a sperm or an oocyte slips from the holding pipette. It is crucial to have redundancies in emergency stop mechanisms and critical sensing modalities (vision and force). Furthermore, a rigorous validation process will be required. Before a completely autonomous system can be extensively used, regulatory bodies would likely require evidence that it is not inferior to human operators across a broad range of scenarios. This may involve multicenter trials or, at the very least, thorough observational studies under regulatory supervision. Another challenge is gaining the trust of patients and practitioners. Patients with infertility frequently develop a rapport with the embryologists who handle their gametes; initially, the prospect of a machine performing the work may cause unease or anxiety. Evidence of safety, together with education, will be beneficial: for instance, sharing success stories of infants born using automated ICSI or presenting videos that demonstrate the accuracy and gentleness of the robotic movements. Clinicians may also be reluctant to relinquish control. Incorporating user-friendly interfaces that enable embryologists to supervise and take appropriate action is one approach to addressing this concern. A potential future model is illustrated by the remote ICSI example: an expert embryologist could oversee several IVF laboratories remotely, intervening via teleoperation only when the automated system encounters an unusual situation. This would extend the expert's reach while maintaining a layer of human oversight [31].

Adapting to various clinical situations presents another difficulty. Patients undergoing IVF vary considerably. Older patients may have more delicate oocytes; some patients may have very few sperm, necessitating careful handling of tiny volumes; others may have nonstandard oocytes (e.g., giant oocytes in specific situations, or oocytes with a hardened zona following ovarian tissue transplantation). To address these edge cases, automated systems must be adaptable. AI-driven adjustments may be necessary for this purpose. An oocyte's quality or zona thickness, for example, may be evaluated in real time by AI image analysis, which could then adjust injection parameters (more piezo pulses for a thick zona, or extra-gentle handling for a delicate oocyte). Modular designs

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and various pipette types or modes that the operator can choose from (such as a "fragile oocyte" mode with more cautious settings) may also be involved. It remains difficult to ensure that automation can manage the entire range of cases that expert embryologists handle.

Another consideration is the financial aspect. Automation may reduce costs over time due to labor savings and increased efficiency, but the initial cost of such equipment is significant. IVF clinics must be persuaded of the return on investment (ROI). High-volume laboratories or research facilities that can afford it may be the first to adopt automated ICSI. Smaller clinics may be able to adopt the technology as it matures and potentially becomes more affordable (for instance, by producing microfluidic chips in large quantities or making precision robots more widely available). A larger patient population will be able to access reproductive treatments if automation successfully reduces manual laboratory work and increases per-cycle success rates.

Significant concerns exist regarding transparency and accountability when AI is used in gamete and embryo selection. To adequately counsel patients, clinicians need to know exactly how an algorithm selects a particular sperm or evaluates an embryo. To retain oversight, regulatory frameworks will likely require a "human in the loop" for critical clinical judgments in the early stages. Several of these ethical issues in ART were highlighted by Zammit (2023), including algorithmic bias, data privacy concerns with cloud-based platforms, and the significance of maintaining the dignity of human reproduction in the face of increasing automation [52]. Transparent communication and practical measures are needed to address these concerns. For instance, employing localized, secure servers helps safeguard patient privacy, while training models on diverse medical datasets can reduce bias. Ultimately, automation seeks to support fertility teams rather than to replace them. The empathy and nuanced decision-making of healthcare providers are irreplaceable, even as automated systems take over repetitive laboratory tasks.

Future developments could involve the integration of time-lapse embryo imaging directly into the automated ICSI workflow. Advanced prognostic AI could evaluate unfertilized oocytes to predict their developmental potential. Armed with these real-time analytics, an automated system could assist in triage decisions, such as prioritizing specific oocytes or identifying cases where the prognosis is too poor to warrant injection. Although adjusting clinical strategies on the basis of automated predictions raises significant ethical questions and remains speculative, it represents a clear technical direction as predictive accuracy improves. Another future direction involves combining gene editing or other advanced manipulations with ICSI in a streamlined automated process (for research or clinical applications under proper regulation). If CRISPR or other tools are to be used on gametes or zygotes, an automated system might precisely inject the gene-editing reagents immediately after sperm injection, thereby minimizing additional handling, a task considerably more difficult to coordinate manually.

In the shorter term, one concrete direction involves refining the integration of automated ICSI with preimplantation genetic testing (PGT) workflows. Automated systems could potentially perform embryo biopsy or operate in coordination with biopsy robots. In addition, because cryopreservation is frequently performed (whether of sperm, oocytes, or embryos), having a robotic system that can seamlessly transfer an embryo from culture to a vitrification device (as in the patent by Millan et al. [50]) could ensure that embryos are frozen with minimal stress and operator variability.

Finally, training and workforce implications warrant consideration. Embryologists are likely to shift away from tedious benchwork and toward system oversight, quality control, and managing complex cases as labs become more automated. Consequently, training programs will need to evolve, teaching students how to operate automated technologies and interpret AI diagnostics in addition to conventional embryology methods. By automating high-volume repetitive procedures, these tools address industry-wide personnel shortages and burnout, rather than replacing embryologists [12]. During a transitional phase when manual and automated workflows will unavoidably overlap, automation will free embryologists to make complex clinical decisions and oversee patient care. During this time, maintaining proficiency in both approaches will be essential. Professional guidelines may emerge on how to validate an automated system before clinical use and how to maintain it (e.g., calibration schedules and proficiency testing using dummy oocytes).

A 2026 proof-of-concept study evaluated a sequential automated workflow involving sperm preparation, oocyte handling, and ICSI in 11 cases [53]. In the automated arm, 45 of 70 injected oocytes fertilized (64.3%), 19 of 45 zygotes formed usable blastocysts (42.2%), and embryo transfers resulted in five live births [53]. Although the corresponding descriptive outcomes were higher with manual procedures, the sample was too small for statistical comparison, and some automated steps required direct operator intervention or digital control. These findings demonstrate feasibility rather than superiority and underscore the need for independent replication, larger comparative studies, and transparent reporting of which steps are autonomous, digitally controlled, or manually performed.

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Overall, the future of ICSI and ART laboratory automation is promising but will require careful navigation of challenges. The next milestones will likely be incremental: an increase in the number of fully automated ICSI cases reported in the literature, development of combined sperm selection-injection devices, and perhaps the first head-to-head clinical trial of automated versus manual ICSI. Each success will pave the way for broader acceptance. If the challenges of safety, acceptance, and cost are addressed, the coming decades may witness an IVF laboratory that differs considerably from those of today, perhaps more akin to a high-tech incubation box that runs largely on its own, supervised by clinicians from a control station. Such a laboratory might function in settings such as a hospital with few specialists in a developing nation. The primary ethical objective nevertheless remains unchanged: assisting patients in having safe, healthy infants. Autonomy is not the objective in itself; it is merely a means to that end. Fertility treatments can be made more accurate, reliable, and accessible through the careful integration of robotics and digital technologies with human clinical expertise.

5. Conclusions

Automated ICSI has rapidly progressed from a theoretical concept to practical clinical application. At present, sophisticated sperm injection tasks can be performed by robotic devices and AI models with an accuracy comparable to that of a human embryologist. Normal fertilization rates and healthy live births have already been achieved in early clinical applications, supporting the feasibility of the strategy in practice [17]. Although relatively new, the technology is advancing rapidly. IVF laboratories are gradually moving toward automated, highly standardized operations owing to ongoing advances in micromanipulation, computer vision, and real-time control software.

Rather than replacing human expertise, automation seeks to enhance reproductive medicine. In practice, automated ICSI can serve as a laboratory tool to reduce procedural variability, increase throughput, and alleviate personnel shortages. Embryologists will continue to play crucial roles in direct patient interaction, complex case management, and system oversight. Clinical confidence will inevitably spur wider adoption as more evidence demonstrates these systems' reliability and safety. By reducing reliance on highly specialized manual skills and standardizing clinical outcomes, this change could substantially broaden access to fertility care.

Significant obstacles remain, most notably ensuring that automated platforms can accommodate the great diversity of clinical samples while maintaining stringent quality control. To maintain the safety and ethical integrity of robotic embryo creation, ethical and regulatory standards must keep up with these technological developments [52]. In this process, interdisciplinary collaboration among engineers, reproductive biologists, physicians, and ethicists will be essential.

Ultimately, automated ICSI represents a substantial shift in assisted reproduction. The first successful live births from robotic injections, AI-guided sperm selection, and real-time computer vision exemplify achievements that point to a future in which human judgment and machine prediction collaborate to improve fertility treatment. A large portion of the IVF laboratory will likely be automated or semi-automated over the next decade, resulting in an intelligent system that directly supports the embryologist. This combination can help more patients build families, increase success rates, and reduce procedural risks. ICSI originated as a pioneering manual technique that revolutionized the treatment of infertility [1], but it is now entering a phase in which automation and remote connectivity [31] may make IVF substantially more reliable and accessible. The ethical soundness and efficacy of this technological advancement may be strengthened by a sustained emphasis on clinical evidence and patient safety.

List of Abbreviations

AI	Artificial Intelligence
AR	Augmented Reality
ART	Assisted Reproductive Technology
DDS	Data Distribution Service
DNA	Deoxyribonucleic Acid
ICSI	Intracytoplasmic Sperm Injection
IVF	In Vitro Fertilization
NOA	Non-Obstructive Azoospermia
PGT	Preimplantation Genetic Testing
ROI	Return on Investment
ROS2	Robot Operating System 2

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Conceptualization, investigation, data curation, visualization, and writing—original draft preparation: M.M.; Supervision and writing—review & editing: M.I. The authors have read and agreed to the published version of the manuscript.

Availability of Data and Materials

No new datasets were generated or analyzed in this review. All information discussed herein is available in the cited publications.

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Conflicts of Interest

The authors declare no conflicts of interest.

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AI Declaration

Language correction and text refinement were performed using OpenAI ChatGPT 5.x. The authors evaluated and approved all scientific interpretations, findings, and the final content and take full responsibility for the accuracy, originality, integrity, and scientific content of the manuscript.

References

[1] Palermo, G.; Joris, H.; Devroey, P.; Van Steirteghem, A.C. Pregnancies after Intracytoplasmic Injection of Single Spermatozoon into an Oocyte. *Lancet* **1992**, *340*, 17–18. [CrossRef] [PubMed]

[2] Banker, M.; Dyer, S.; Chambers, G.M.; Ishihara, O.; Kupka, M.; de Mouzon, J.; Adamson, F.Z.-H.D. International Committee for Monitoring Assisted Reproductive Technologies (ICMART): World Report on Assisted Reproductive Technologies, 2013. *Fertil. Steril.* **2021**, *116*, 741–756. [CrossRef] [PubMed]

[3] Rubino, P.; Vigano, P.; Luddi, A.; Piomboni, P. The ICSI Procedure from Past to Future: A Systematic Review of the Most Controversial Aspects. *Hum. Reprod. Update* **2016**, *22*, 194–227. [CrossRef] [PubMed]

[4] Boulet, S.L.; Mehta, A.; Kissin, D.M.; Warner, L.; Kawwass, J.F.; Jamieson, D.J. Trends in Use of and Reproductive Outcomes Associated with Intracytoplasmic Sperm Injection. *JAMA* **2015**, *313*, 255–263. [CrossRef] [PubMed]

[5] O'Neill, C.L.; Chow, S.; Rosenwaks, Z.; Palermo, G.D. Development of ICSI. *Reproduction* **2018**, *156*, F51–F58. [CrossRef] [PubMed]

[6] Tiegs, A.W.; Scott, R.T. Evaluation of Fertilization, Usable Blastocyst Development and Sustained Implantation Rates According to Intracytoplasmic Sperm Injection Operator Experience. *Reprod. Biomed. Online* **2020**, *41*, 19–27. [CrossRef] [PubMed]

[7] Nagy, Z.P.; Liu, J.; Joris, H.; Bocken, G.; Desmet, B.; van Ranst, A.; Vankelecom, A.; Devroey, P.; van Steirteghem, A.C. The influence of the Site of Sperm Deposition and Mode of Oolemma Breakage at Intracytoplasmic Sperm Injection on Fertilization and Embryo Development Rates. *Hum. Reprod.* **1995**, *10*, 3171–3177. [CrossRef] [PubMed]

[8] Palermo, G.D.; Alikani, M.; Bertoli, M.; Colombero, L.T.; Moy, F.; Cohen, J.; Rosenwaks, Z. Oolemma Characteristics in Relation to Survival and Fertilization Patterns of Oocytes Treated by Intracytoplasmic Sperm Injection. *Hum. Reprod.* **1996**, *11*, 172–176. [CrossRef] [PubMed]

[9] Dumoulin, J.M.; Coonen, E.; Bras, M.; Bergers-Janssen, J.M.; Ignoul-Vanvuchelen, R.C.M.; van Wissen, L.C.P.; Geraedts, J.P.M.; Evers, J.L.H. Embryo Development and Chromosomal Anomalies after ICSI: Effect of the Injection Procedure. *Hum. Reprod.* **2001**, *16*, 306–312. [CrossRef] [PubMed]

[10] Rienzi, L.; Ubaldi, F.; Martinez, F.; Iacobelli, M.; Minasi, M.G.; Ferrero, S.; Tesarik, J.; Greco, E. Relationship Between Meiotic Spindle Location with Regard to the Polar Body Position and Oocyte Developmental Potential after ICSI. *Hum. Reprod.* **2003**, *18*, 1289–1293. [CrossRef] [PubMed]

[11] Alikani, M.; Go, K.J.; McCaffrey, C.; McCulloh, D.H. Comprehensive Evaluation of Contemporary Assisted Reproduction Technology Laboratory Operations to Determine Staffing Levels That Promote Patient Safety and Quality Care. *Fertil. Steril.* **2014**, *102*, 1350–1356. [CrossRef] [PubMed]

[12] Sciorio, R.; Aiello, R.; Janssens, R. Considerations on Staffing Levels for a Modern Assisted Reproductive Laboratory. *JBRA Assist. Reprod.* **2023**, *27*, 120–130. [CrossRef] [PubMed]

[13] Pujol, A.; García, D.; Obradors, A.; Rodríguez, A.; Vassena, R. Is There a Relation Between the Time to ICSI and the Reproductive Outcomes? *Hum. Reprod.* **2018**, *33*, 797–806. [CrossRef] [PubMed]

[14] Hansen, M.; Bower, C.; Milne, E.; de Klerk, N.; Kurinczuk, J.J. Assisted Reproductive Technologies and the Risk of Birth Defects—A Systematic Review. *Hum. Reprod.* **2005**, *20*, 328–338. [CrossRef] [PubMed]

[15] Cherouveim, P.; Velmahos, C.; Bormann, C.L. Artificial Intelligence for Sperm Selection—A Systematic Review. *Fertil. Steril.* **2023**, *120*, 24–31. [CrossRef] [PubMed]

[16] Wang, Z.; Feng, C.; Ang, W.T.; Tan, S.Y.M.; Latt, W.T. Autofocusing and Polar Body Detection in Automated Cell Manipulation. *IEEE Trans. Biomed. Eng.* **2017**, *64*, 1099–1105. [CrossRef] [PubMed]

[17] Costa-Borges, N.; Munné, S.; Albó, E.; Mas, S.; Castelló, C.; Giralt, G.; Lu, Z.; Chau, C.; Acacio, M.; Mestres, E. First Babies Conceived with Automated Intracytoplasmic Sperm Injection. *Reprod. Biomed. Online* **2023**, *47*, 103237. [CrossRef] [PubMed]

[18] ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine. The Vienna Consensus: Report of an Expert Meeting on the Development of ART Laboratory Performance Indicators. *Reprod. Biomed. Online* **2017**, *35*, 494–510. [PubMed]

[19] VerMilyea, M.; Hall, J.M.M.; Diakiw, S.M.; Johnston, A.; Nguyen, T.; Perugini, D.; Miller, A.; Picou, A.; Murphy, A.P.; Perugini, M. Development of an Artificial Intelligence-Based Assessment Model

ACCEPTED

for Prediction of Embryo Viability Using Static Images Captured by Optical Light Microscopy During IVF. *Hum. Reprod.* **2020**, *35*, 770–784. [CrossRef] [PubMed]

[20] Yoshida, N.; Perry, A.C. Piezo-Actuated Mouse Intracytoplasmic Sperm Injection (ICSI). *Nat. Protoc.* **2007**, *2*, 296–304. [CrossRef] [PubMed]

[21] Yanagida, K.; Katayose, H.; Yazawa, H.; Kimura, Y.; Konnai, K.; Sato, A. The Usefulness of a Piezo-Micromanipulator in Intracytoplasmic Sperm Injection in Humans. *Hum. Reprod.* **1999**, *14*, 448–453. [CrossRef] [PubMed]

[22] Takeuchi, S.; Minoura, H.; Shibahara, T.; Shen, X.; Futamura, N.; Toyoda, N. Comparison of Piezo-Assisted Micromanipulation with Conventional Micromanipulation for Intracytoplasmic Sperm Injection into Human Oocytes. *Gynecol. Obstet. Invest.* **2001**, *52*, 158–162. [CrossRef] [PubMed]

[23] Zander-Fox, D.; Lam, K.; Pacella-Ince, L.; Tully, C.; Hamilton, H.; Hiraoka, K.; McPherson, N.O.; Tremellen, K. PIEZO-ICSI Increases Fertilization Rates Compared with Standard ICSI: A Prospective Cohort Study. *Reprod. Biomed. Online* **2021**, *43*, 404–412. [CrossRef] [PubMed]

[24] Caddy, M.; Popkiss, S.; Weston, G.; Vollenhoven, B.; Rombauts, L.; Green, M.; Zander-Fox, D. PIEZO-ICSI Increases Fertilization Rates Compared with Conventional ICSI in Patients with Poor Prognosis. *J. Assist. Reprod. Genet.* **2023**, *40*, 389–398. [CrossRef] [PubMed]

[25] Fernández, J.; Pedrosa, C.; Vergara, F.; Nieto, A.I.; Quintas, A.; Fernández, A.; Moyano, C.; Fernández, A.; Ponce, J. A New Oocyte-Holding Pipette for intracytoplasmic Sperm Injection Without Cytoplasmic Aspiration: An Experimental Study in Mouse Oocytes. *Reprod. Biol.* **2020**, *20*, 584–588. [CrossRef] [PubMed]

[26] Tan, Z.; Zhang, D. Interactive OT Gym: A Reinforcement Learning-Based Interactive Optical Tweezer (OT)-Driven Microrobotics Simulation Platform. In Proceedings of the IEEE International Conference on Robotics and Automation (ICRA), Atlanta, GA, USA, 19–23 May 2025; pp. 1–7. [CrossRef]

[27] Lu, Z.; Zhang, X.; Leung, C.; Esfandiari, N.; Casper, R.F.; Sun, Y. Robotic ICSI (Intracytoplasmic Sperm Injection). *IEEE Trans. Biomed. Eng.* **2011**, *58*, 2102–2108. [CrossRef] [PubMed]

[28] Leung, C.; Lu, Z.; Esfandiari, N.; Casper, R.F.; Sun, Y. Automated Sperm Immobilization for Intracytoplasmic sperm Injection. *IEEE Trans. Biomed. Eng.* **2011**, *58*, 935–942. [CrossRef] [PubMed]

[29] Zhang, Z.; Dai, C.; Huang, J.; Wang, X.; Liu, J.; Ru, C.; Pu, H.; Xie, S.; Zhang, J.; Moskovtsev, S.; et al. Robotic Immobilization of Motile Sperm for Clinical Intracytoplasmic Sperm Injection. *IEEE Trans. Biomed. Eng.* **2019**, *66*, 444–452. [CrossRef] [PubMed]

[30] Mor, A.; Zhang, M.; Esencan, E.; Seli, E. A Step Towards the Automation of Intracytoplasmic Sperm Injection: Real Time Confirmation of Mouse and Human Oocyte Penetration and Viability by Electrical Resistance Measurement. *Fertil. Steril.* **2020**, *113*, 234–236. [CrossRef] [PubMed]

[31] Mendizabal-Ruiz, G.; Chavez-Badiola, A.; Hernández-Morales, E.; Valencia-Murillo, R.; Ocegueda-Hernández, V.; Costa-Borges, N.; Mestres, E.; Acacio, M.; Matia-Algué, Q.; Farías, A.F.-S.; et al. A Digitally Controlled, Remotely Operated ICSI System: Case Report of the First Live Birth. *Reprod. Biomed. Online* **2025**, *50*, 104943. [CrossRef] [PubMed]

[32] Lattin, M.T.; Djandji, A.S.; Kronfeld, M.T.; Samsel, T.; Ling, R.; Ciskanik, M.; Sadowy, S.; Forman, E.J.; Williams, Z. Development and Validation of an Automated Robotic System for Preparation of Embryo Culture Dishes. *Fertil. Steril.* **2024**, *122*, 297–303. [CrossRef] [PubMed]

[33] Palermo, G.D. Automated Intracytoplasmic Sperm Injection Assisted Fertilization System. EP Patent No. 2,838,987, 6 March 2019.

[34] Macenski, S.; Foote, T.; Gerkey, B.; Lalancette, C.; Woodall, W. Robot Operating System 2: Design, Architecture, and Uses in the Wild. *Sci. Robot.* **2022**, *7*, eabm6074. [CrossRef] [PubMed]

[35] Park, J.; Delgado, R.; Choi, B.W. Real-Time Characteristics of ROS2 in Multi-Agent Robot Systems: An Empirical Study. *IEEE Access* **2020**, *8*, 154637–154651. [CrossRef]

[36] Mendizabal-Ruiz, G.; Chavez-Badiola, A.; Aguilar Figueroa, I.; Nuño, V.M.; Farias, A.F.-S.; Valencia-Murilloa, R.; Drakeley, A.; Garcia-Sandoval, J.P.; Cohen, J. Computer Software (SiD) Assisted Real-Time Single Sperm Selection Associated with Fertilization and Blastocyst Formation. *Reprod. Biomed. Online* **2022**, *45*, 703–711. [CrossRef] [PubMed]

[37] Baldini, D.; Ferri, D.; Baldini, G.M.; Lot, D.; Catino, A.; Vizziello, D.; Vizziello, G. Sperm Selection for ICSI: Do We Have a Winner? *Cells* **2021**, *10*, 3566. [CrossRef] [PubMed]

[38] Chen, D.; Sun, M.; Zhao, X. Oocytes Polar Body Detection for Automatic Enucleation. *Micromachines* **2016**, *7*, 27. [CrossRef] [PubMed]

[39] Wang, Y.; Liu, Y.; Sun, M.; Zhao, X. Deep-Learning-Based Polar-Body Detection for Automatic Cell Manipulation. *Micromachines* **2019**, *10*, 120. [CrossRef] [PubMed]

[40] Yagi, N.; Tsuji, H.; Morimoto, T.; Maekawa, T.; Mizuta, S.; Ishikawa, T.; Hata, Y. Rupture Prediction for Microscopic Oocyte Images of Piezo Intracytoplasmic Sperm Injection by Principal Component Analysis. *J. Clin. Med.* **2022**, *11*, 6546. [CrossRef] [PubMed]

[41] Tang, T.; Hosokawa, Y.; Hayakawa, T.; Tanaka, Y.; Li, W.; Li, M.; Yalikun, Y. Rotation of Biological Cells: Fundamentals and Applications. *Engineering* **2021**, *10*, 110–126. [CrossRef]

[42] Johnson, W.; Dai, C.; Liu, J.; Wang, X.; Luu, D.K.; Zhang, Z.; Ru, C.; Zhou, C.; Tan, M.; Pu, H.; et al. A Flexure-Guided Piezo Drill for Penetrating the Zona Pellucida of Mammalian Oocytes. *IEEE*

ACCEPTED

Trans. Biomed. Eng. **2018**, *65*, 678–686. [CrossRef] [PubMed]

[43] Mohamed, M.; Kachi, K.; Motoya, K.; Ikeuchi, M. Fast and Accurate Sperm Detection Algorithm for Micro-TESE in NOA Patients. *Bioengineering* **2025**, *12*, 601. [CrossRef] [PubMed]

[44] Mohamed, M.; Ezaki, Y.; Kawagoe, Y.; Kawamura, K.; Ikeuchi, M. AI-Based Augmented Reality Microscope for Real-Time Sperm Detection and Tracking in Micro-TESE. *Bioengineering* **2026**, *13*, 102. [CrossRef] [PubMed]

[45] Chaplia, O.; Mathyk, B.A.; Nichols-Burns, S.; Basar, M.; Halicigil, C. Beyond Earth's Bounds: Navigating the Frontiers of Assisted Reproductive Technologies (ART) in Space. *Reprod. Biol. Endocrinol.* **2024**, *22*, 123. [CrossRef] [PubMed]

[46] Wang, W.; Liu, X.; Gelinas, D.; Ciruna, B.; Sun, Y. A Fully Automated Robotic System for Microinjection of Zebrafish Embryos. *PLoS ONE* **2007**, *2*, e862. [CrossRef] [PubMed]

[47] Guo, Z.; Ai, N.; Ge, W.; Xu, Q. Design of an Automated Robotic Microinjection System for Batch Injection of Zebrafish Embryos and Larvae. *Microsyst. Nanoeng.* **2024**, *10*, 20. [CrossRef] [PubMed]

[48] Nan, Z.; Xu, Q.; Zhang, Y.; Ge, W. Force-Sensing Robotic Microinjection System for automated Multi-Cell Injection with Consistent Quality. *IEEE Access* **2019**, *7*, 55543–55553. [CrossRef]

[49] Chavez Badiola, A. System for Real-Time Automatic Quantitative Evaluation, Evaluation and/or Ranking of Individual Sperm, Intended for Intracytoplasmic Sperm Injection (ICSI) and Other Fertilization Procedures, Which Allows the Selection of a Single Sperm. European Patent Application No. EP4249892A1, 27 September 2023. Available online: https://patents.google.com/patent/EP4249892A1/en (accessed on 20 October 2026).

[50] Millan, C.; Flores-Saiffe Farias, A.; Mendizabal-Ruiz, G.; Silvestri, G.; Manuel Medina Perez, V.; Martínez, D.; Cohen, J.; Chaves-Badiola, A.; Murray, A. Robotic Sperm Preparation in an Intelligent Automated in vitro Fertilization and Intracytoplasmic Sperm Injection Platform. U.S. Patent No. 12,178,475, 2 February 2024. Available online: https://patents.google.com/patent/US12178475B1/en (accessed on 20 October 2026).

[51] Mendizabal-Ruiz, G.; Chavez-Badiola, A.; Murray, A.; Cohen, J.; Flores-Saiffe Farias, A.; Millan, C.; Valencia-Murillo, R.; Ocegueda Hernandez, V.C.; Silvestri, G.; Costa-Borges, N.; et al. Autonomous Vitrification in an Intelligent Automated In Vitro Fertilization and Intracytoplasmic Sperm Injection Platform. U.S. Patent No. US12226125B2, 18 February 2025.

[52] Zammit, R. Ethical Issues of Artificial Intelligence & Assisted Reproductive Technologies. *Int. J. Prenat. Life Sci.* **2023**, In press. 1–24. [CrossRef]

[53] Chavez-Badiola, A.; Mendizabal-Ruiz, G.; Flores-Saiffe Farias, A.; Costa-Borges, N.; Murray, A.; Alikani, M.; Silvestri, G.; Millan, C.; Hernández-Morales, E.; Valencia-Murillo, R.; et al. Automated Oocyte Retrieval, Denudation, Sperm Preparation, and ICSI in the IVF Laboratory: A Proof-of-Concept Study and Report of the First Live Births. *Hum. Reprod.* **2026**, *41*, 214–230. [CrossRef] [PubMed]

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