

Automation in Intra cytoplasmic Sperm Injection (ICSI)

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ICSI is a clinical procedure performed worldwide in fertility clinics, requiring pick-up of a single sperm and insertion of it into an oocyte (i.e., egg cell). Since its invention 20 years ago, ICSI has been conducted manually by a handful of highly skilled embryologists; however, success rates vary significantly among clinics due to poor reproducibility and inconsistency across operators. (1)

ICSI is a procedure which requires selecting a good sperm based on WHO criteria and injecting that sperm into an oocyte. Use of ICSI is significant in the following scenarios, (2) 1. Very low sperm count 2. Poor Morphology 3. Very few or none eggs fertilized with previous IVF 4. Sperms collected surgically to be used (TESA). 5. Use of frozen sperms not of the best quality. 6. The embryos needed to be tested genetically. In the past two decades since its invention, ICSI has been conducted manually by highly skilled embryologists who consider the eyepieces of a microscope while dexterously controlling multiple devices (e.g., micromanipulators, pump, microscope stage). However, long training, stringent skill requirements, low success rates from poor reproducibility (e.g., success rates vary from 50% to 80% in IVF clinics in North America), and inconsistency among operators in manual operation call for the reduction of human involvement and automated ICSI. (1)

Apart from being labour intensive this procedure requires a learning curve as the outcome depends partly on inherent technical difficulty and partly on the heterogeneity of the oocytes. (3) Presently few KPIs are assessed which ensure that the ICSI performed by the operator are within normal limits. They are (but not restricted to) fertilization rate, Degeneration rate, cleavage rate and blastulation rate. There is a huge variability seen in these KPI's which can be overcome by automating the procedure - ICSI. The aim would be to develop an automated system which can effectively select, Immobilise and inject sperm in the cytoplasm of the oocyte.

Since the introduction of ICSI several studies have been conducted to evaluate the immobilization of spermatozoa prior to ICSI as a method to induce sperm plasma

membrane damage before ICS. Although the use of motile sperm cells instead of immobilized sperm has been promoted in the past (9), most studies agree that the use of immobilized sperm is necessary to provoke the processes needed prior to fertilization (10).

Attempts have been made to automate ICSI and promising observation have been recorded. The system achieved a sperm tail visual tracking rate of 96%, a sperm immobilization success rate of 88.2%, and an average time of 2-3 seconds per immobilization. (4) Causes of failed cases were: (a) micropipette disturbed the culture medium, which in turn displaced the sperm from the computed immobilization location; (b) sperm was not immobilized as it was swimming above the substrate surface; (c) sperm tail was not in the required immobilization orientation; and sperm evaded the micropipette by (d) changing its tail orientation or (e) increasing its speed. (4)

Several algorithms have been developed in the field of computer-assisted sperm analysis (CASA) to track sperm trajectories, measure sperm velocity, and evaluate sperm energetics (5), (6). Prior work for estimating the direction of a sperm tail used the minor and major axes of the sperm head's morphology (7). The sperm head, however, has a wide variety of shapes (8)]. Thus, the approach does not always provide the correct direction of the sperm tail. Despite the considerable progress made in CASA, automated detection and tracking of sperm tails have not been explored. Also, CASA did not have the ability to differentiate between immotile sperms and debris.

Although, not all is lost. The automated robotic system developed by C.Leung et al can conduct human sperm immobilization with a high success rate. It is a critical procedure for automated human ICSI. (4) The challenge is to keep exploring and find innovative ways to automate ICSI to be able to standardize results worldwide.

1. Robotic ICSI (intracytoplasmic sperm injection).

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