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Moving Beyond the Black Box: A Proposed Integrated Clinical AI Scoring (ICAIS) Matrix for Embryo Selection

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Abstract

Background

Embryo selection remains a critical determinant of IVF success. Despite advances in morphology, time-lapse imaging, and preimplantation genetic testing for aneuploidy (PGT-A), implantation failure still occurs in morphologically high-quality and euploid embryos, highlighting limitations in current assessment methods. The current study is a theoretical framework development study based on literature synthesis (2000–2026) from major databases. The proposed Integrated Comprehensive AI-based Implantation Scoring system (ICAIS) comprises three domains: morphology (0–9 points), morphokinetics (0–3 points), and an AI-derived adjustment factor (−2 to +3 points), yielding a total score of 0- 15.The aim is to develop an integrated, transparent scoring system combining morphology, morphokinetics, and artificial intelligence (AI) to improve prediction of embryo implantation potential.

Results

The ICAIS model stratifies embryos into low (0–7), intermediate (8–11), and high (12–15) implantation potential categories. The integrated approach demonstrates improved theoretical discrimination between embryos with similar morphology but different implantation potential, and better alignment with known euploidy and developmental competence patterns.

Conclusion

ICAIS provides a structured and interpretable framework that integrates conventional and AI-based embryo assessment. It has the potential to enhance embryo selection and address unexplained implantation failure, although prospective clinical validation is required.

Keywords

Embryo selection; artificial intelligence; morphokinetics; PGT-A; implantation; IVF

Declarations

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Author contributions

Hassan Maghraby: Protocol/project development; Data analysis; Manuscript writing/editing; Abdulaziz

Belhaj: Data collection or management; Data analysis; Manuscript writing/editing; Rogaya Aborawi: Data collection or management; Data analysis; Heba Maghraby: Protocol/project development; Manuscript writing/editing; Mohamed Elmahdy: Manuscript writing/editing; supervision; Nehal Ade: Manuscript writing/editing; supervision. All authors read and approved the final manuscript.

Ethics approval

Not applicable; it is a concept perspective article.

Consent to participate

Not applicable; no patients included.

Data availability

No new datasets were generated or analyzed for this concept/perspective article. The information used to develop the proposed selection model was derived from previously published literature, with AI-assisted support in literature retrieval and synthesis. The relevant sources are cited in the manuscript.

Background

Embryo selection remains the foundational rate-limiting step determining clinical success in assisted reproductive technology (ART).[1] For decades, standard laboratory practice has relied heavily on manual, subjective morphological grading at the blastocyst stage.[2] The traditional Gardner and Schoolcraft system, which prioritizes blastocyst expansion alongside the cell density and cohesive structure of the inner cell mass (ICM) and trophectoderm (TE), serves as the global clinical benchmark.[3] While universally adopted, static morphology possesses inherent biological limitations. It provides merely a snapshot of a highly dynamic developmental continuum, explaining only a moderate proportion of the variance in implantation success. [4] Clinicians frequently encounter the therapeutic dilemma of morphologically excellent blastocysts failing to implant, or conversely, poor-grade embryos resulting in healthy live births.

To overcome these visual limitations, preimplantation genetic testing for aneuploidy (PGT-A) was introduced to directly evaluate chromosomal copy-number variations.[5] While trophectoderm biopsy has undeniably improved clinical pregnancy rates per transfer and lowered miscarriage rates in specific patient populations, its status as a routine screening tool for all IVF patients remains a subject of intense global debate.[6] The heavy reliance on PGT-A introduces substantial challenges, including its high cost, operational invasiveness, potential long-term epigenetic impacts on the blastocyst, and the biological confounding factors of chromosomal mosaicism and sample bias.[7] Consequently, there is an urgent clinical mandate to pioneer non-invasive, objective, and highly predictive biomarkers capable of capturing overall embryo viability without cellular disruption.

Recent technological shifts have introduced two powerful computational paradigms to the IVF laboratory: time-lapse imaging (TLI) systems and deep learning artificial intelligence (AI) networks.[8] TLI tracks early cellular division kinetics, mapping vital chronological milestones such as time to two-cell (t2), three-cell (t3), and five-cell (t5) stages, alongside blastulation windows.[9] Concurrently, computer-vision AI algorithms can identify subtle, subvisual architectural features within the blastocyst that elude the human eye.[10] However, the contemporary implementation of AI in embryology faces a distinct hurdle: the "black box" phenomenon.[11] Most proprietary AI platforms generate an uninterpretable mathematical probability score, depriving embryologists and clinicians of the underlying biological rationale behind the machine's decision.[11] Furthermore, these closed systems typically evaluate isolated data domains, ignoring maternal physiological variables or manual morphological metrics.

To bridge this clinical-technological divide, we introduce the concept of the "Aneuploidy Gap" defined as the mathematical and biological discordance between a blastocyst's visible morphological grade and its underlying chromosomal or metabolic competence. To systematically close this gap, this study proposes the Integrated Clinical and AI Scoring System (ICAIS). By engineering an additive, fully transparent, multi-domain matrix, the ICAIS model

integrates conventional morphology, dynamic developmental morphokinetics, and an AI-derived predictive layer into a single interpretable clinical score, standardizing embryo prioritization and modernizing evidence-based reproductive medicine. Crucially, because this framework is constructed and driven entirely by AI-assisted search and extraction of published literature, without active patient enrollment, exhaustive formal systematic review registries, or real-world clinical testing, ICAIS remains a purely hypothetical concept awaiting prospective validation in real clinical cohorts.

Methods

Literature Search and Information Extraction Protocol

The conceptual development of the ICAIS framework was executed utilizing an AI-powered literature search and targeted information extraction strategy rather than a formal, protocol-registered systematic review. Large language modeling and search algorithms were utilized to execute a rapid, high-yield sweep of major electronic databases, including PubMed, Scopus, and Web of Science, covering literature published between January 2000 and May 2026. The technical search syntax focused on Boolean combinations of key terms: ("embryo selection" OR "blastocyst grading") AND ("artificial intelligence" OR "deep learning") AND ("morphokinetics" OR "time-lapse") AND ("PGT-A" OR "euploidy").

The AI-driven extraction prioritized peer-reviewed clinical trials, retrospective cohorts, and recent 2025–2026 computer-vision validation studies that detailed explicit mathematical correlations between blastocyst structural anomalies, kinetic milestones, and clinical implantation rates. Studies involving non-human models, non-English publications, or unverified conference abstracts were filtered out during data extraction. The extracted parameters were then utilized by the authors to manually map, weight, and assemble the core scoring domains of the theoretical model.

Model Architecture and Algorithmic Construct

The ICAIS model operates on a weighted, additive scoring matrix designed to give clinicians immediate insight into the specific biological variables driving the final score. The model synthesizes three independently calculated domains into a single score ranging from 0 to 15:

1. **Morphology Domain (0–9 points):** Establishes the foundational structural weight. It mathematically converts standard blastocyst expansion (stages 1–6) alongside ICM and TE quality (Grades A, B, C) into a numerical scale, further penalized or rewarded based on blastomere symmetry and fragmentation indices.
2. **Morphokinetics Domain (0–3 points):** Refines the static score by analyzing dynamic kinetic intervals derived from time-lapse monitoring. Points are allocated based on adherence to established optimal cleavage windows (e.g., t5 - t2 intervals) and synchronicity markers.

3. **AI-Derived Predictive Adjustment Factor (-2 to +3 points):** Functions as a higher-order non-linear correction layer. This factor integrates automated pixel-level pattern recognition from convolutional neural networks (CNNs) calibrated against multi-center known implantation delivery datasets. This layer modifies the clinical score to account for subvisual structural variations.

Theoretical Optimization and Implantation Stratification

To evaluate the theoretical performance of the model, a simulation matrix was designed using published datasets of known euploid non-implanting embryos and aneuploid/mosaic blastocysts. Sensitivity analyses were performed to evaluate the mathematical stability of the model across varying weight distributions, ensuring that the AI adjustment layer optimizes prediction without overriding critical clinical observations.

Methodological Boundary Note: Because the algorithmic parameters, domain weightings, and score distributions are extracted from aggregated historical data via a narrative AI search rather than fresh clinical testing, this framework is restricted to a theoretical simulation. The framework lacks direct, real patient validation at this stage; hence, all outcome definitions, sensitivity matrices, and prospective predictive values remain entirely hypothetical pending future clinical application.

Results

Framework Synthesis Outcomes

The structured evidence extraction confirmed that while conventional manual morphology remains the most practical baseline predictor, it leaves a massive proportion of implantation variability unexplained.[12] Time-lapse morphokinetic algorithms significantly reduce inter-observer variability and flag cleavage anomalies (such as direct cleavage or irregular cytokinesis) that correlate with chromosomal instability.[13] Furthermore, recent clinical datasets from 2025 and 2026 demonstrate that deep learning systems trained on static or video blastocyst images achieve high area-under-the-curve (AUC) values for predicting clinical pregnancy, providing a layer of objective verification that complements human embryologists.[14]

ICAIS Model Construction and Parameter Weighting

The hierarchical distribution of the ICAIS matrix ensures that computational analytics augment, rather than replace, clinical judgment. The detailed allocation of components, parameters, and descriptive parameters is outlined in Table 1.

Table 1. ICAIS scoring components

Domain	Evaluated Parameters	Score Range	Clinical and Biological Description
Morphology	ICM quality, TE grade, expansion stage, blastomere symmetry, fragmentation index	0 to 9	Establishes the primary structural and macro-architectural base quality of the blastocyst.[12]
Morphokinetics	Kinetic parameters (t2, t3, t5), cleavage synchronicity (S2), blastulation intervals	0 to 3	Refines assessment based on cellular division dynamics and developmental timeline normality.[13]
AI Adjustment	Deep-learning pattern recognition, subvisual pixel analysis, automated viability mapping	-2 to +3	Acts as an objective predictive refinement layer; penalizes hidden defects or rewards subvisual competence.[14]

Predictive Stratification and Clinical Risk Categorization

By executing the additive algorithm, embryos are automatically triaged into three clear, conceptually actionable tiers. This stratification system is designed to assist the IVF team in ordering transfers, counseling patients, or selecting blastocysts for vitrification (Table 2).

Table 2. ICAIS embryo classification system

ICAIS Score	Risk Category	Predicted Implantation Potential & Clinical Actions
12 to 15	High	Strong likelihood of euploidy and optimal implantation probability. Highest priority for single embryo transfer (SET).[16]
8 to 11	Intermediate	Variable clinical outcomes. Requires careful clinical prioritization and consideration of patient-specific co-factors.[17]
0 to 7	Low	High statistical likelihood of aneuploidy, severe developmental arrest, or implantation failure. Deprioritized for clinical use.[18]

Comparative Conceptual Performance

When contrasted against isolated conventional grading frameworks, the multi-domain ICAIS architecture effectively overcomes the clinical ambiguity of "good-quality" blastocysts that exhibit occult developmental or kinetic anomalies. The comparative benefits are synthesized in Table 3.

Table 3. Comparative conceptual performance of selection models

Evaluated Feature	Morphology Only	Time-Lapse + Morphology	Proposed ICAIS Model
Euploid Discrimination	Low to Moderate	Moderate	**High**[18]
Implantation Prediction	Moderate	High	**Very High (Theoretical)**[14]
Methodological Interpretability	High	Moderate	**High (White-Box Design)**[11]
AI Integration	None	Limited	**Full Structured Integration**[11]

Empirical Boundary Note: All outcomes presented in the matrices above describe theoretical parameters optimized from published datasets. Because this grading engine is constructed from literature values without active clinical trial validation or patient context integration, these metrics do not represent real-world clinical performance or established success rates.

Discussion

The introduction of the ICAIS framework provides a conceptually scalable solution to a long-standing challenge in reproductive medicine: the incomplete predictive accuracy of manual blastocyst morphology.[15] As the global IVF community increasingly transitions to single embryo transfer (SET) protocols to minimize multiple gestations, selecting the single most competent blastocyst from a cohort has become paramount.[16] While contemporary approaches rely heavily on either invasive PGT-A or completely closed, black-box AI software, ICAIS offers an

interpretable, clinician-centric model that balances biological transparency with machine-learning precision.[11]

The primary conceptual utility of the ICAIS model lies in its ability to resolve the problem of morphologically identical blastocysts that yield entirely divergent clinical paths.[17] By defining the "Aneuploidy Gap," this framework addresses the subtle micro-architectural or kinetic deviations that escape human vision but are captured by automated computer-vision algorithms.[18] For instance, an embryo graded as a "4AA" might receive a maximum score of 9 in the morphology domain; however, if time-lapse imaging reveals an irregular t3-t2 cleavage window, and the deep-learning network identifies subvisual signs of early cellular degeneration, the morphokinetic and AI domains will apply negative adjustments. This drops the final ICAIS score into an intermediate category, preventing the premature prioritization of a structurally misleading embryo.

Furthermore, the modular and transparent architecture of ICAIS addresses the widespread skepticism among embryologists regarding completely automated AI platforms. By serving as an open methodology, clinicians can instantly audit *why* an embryo received its score, ensuring that human oversight remains central to laboratory workflows.[11] This standardized scoring system can significantly minimize inter-observer and intra-observer variability across different operators and laboratories, stabilizing clinical success rates.[19] Additionally, the open architecture of ICAIS ensures adaptability; future iterations can seamlessly incorporate non-invasive metabolomic signatures from spent embryo culture media or proteomic biomarkers without requiring a complete redesign of the scoring engine.[20]

Study Limitations and Theoretical Boundaries

The fundamental limitation of this study is its entirely theoretical and speculative nature. Because the ICAIS matrix has been developed and driven exclusively from an AI-assisted search and extraction of literature records rather than an exhaustive, protocol-driven systematic review, it may be subject to selection and extraction biases. Furthermore, it has not yet been exposed to, or validated against, any real patient cohorts or prospective clinical laboratory data. Confounding clinical variables such as patient demographics, body mass index, diverse ovarian stimulation protocols, varying culture media formulations, and heterogeneous incubator environments have not been factored into a real-world testing environment. Consequently, the assigned scoring weights and numerical boundaries remain uncalibrated against real clinical outcomes, such as confirmed clinical pregnancy, ongoing pregnancy, or live birth rates. Until large-scale, prospective clinical data are compiled, the ICAIS model must be viewed strictly as a hypothetical blueprint for an open-source, integrated embryo selection framework.

Conclusion

The ICAIS model represents a step forward in digital embryology, providing a novel, transparent, and scalable embryo evaluation matrix. By unifying conventional morphology, time-lapse morphokinetics, and structured AI adjustments into an interpretable white-box framework, this system balances technological innovation with clinical intuition. However, because this model is driven purely by AI-assisted literature extraction without real patient validation, it remains an unvalidated, hypothetical concept. Future research must focus heavily on multi-center clinical testing, machine learning calibration using real-world clinical delivery datasets, and direct comparisons against standard manual blastocyst morphology to convert this theoretical matrix into an active, validated clinical tool.

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Author contributions

Hassan Maghraby: Protocol/project development; Data analysis; Manuscript writing/editing; Abdulaziz Belhaj: Data collection or management; Data analysis; Manuscript writing/editing; Rogaya Aborawi: Data collection or management; Data analysis; Heba Maghraby: Protocol/project development; Manuscript writing/editing; Mohamed Elmahdy: Manuscript writing/editing; supervision; Nehal Ade: Manuscript writing/editing; supervision. All authors read and approved the final manuscript.

Ethics approval

Not applicable; it is a concept perspective article.

Consent to participate

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Data availability

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