

Automation Technique for classification of Human In-Vitro Fertilized (IVF) Embryos using Digital Image Processing Techniques

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Abstract— the identification of infertility problem has evolved the process of in vitro fertilization (IVF) considerably, yet the efficiency of IVF treatment remains relatively poor as considered with the rate of implantation. The main task faced by all specialists and embryologists is the selection of the embryo with the greatest potential for producing a child. Currently doctors can only provide a rough estimation for the viability of embryos by observing their morphological features using a microscope, which is subjective and is often dependent on the individual experience of doctors. In order to improve the odds of a successful pregnancy, one of great procedure to transfer more than one embryo to the uterus. Automated assessment of identifying more potential embryo and elimination of inter- and intra-observer variation. Work is concerned with developing image processing techniques to automate the detection and classification of cells in digital images of day 2 and day 3 embryos for suitability for In Vitro Fertilization (IVF) treatment.

Index Terms—IVF, Potential Embryo, Image Processing, Automated assessment.

I. INTRODUCTION

Medical image processing has evolved a considerable expansion in research field that fascinated expertise from applied mathematics, computer sciences, engineering, biology and even medicine. Many of these applications involve the analysis of cells seen through microscopes like the human embryos for detection of potential/good embryo, classification and monitoring. Typical of these has been the segmentation and classification of blood cells, identifying disease like malaria using medical image processing.

The study is concerned with developing and implementing a system that automatically classifies human embryo cells as seen through a microscope suitable for implantation as shown in Fig.1. These cells are fertilized outside the women's womb. These fertilized eggs are classified as suitable for implantation, using grading schemes that are dependent on their age. Identifying a potential embryo for the implantation is subjective, so transferring more than one embryo will lead Accurate classification of these cells will prevent the mother and baby from acquiring many health problems that might occur due to multi-cell implantation. The work described aims to develop

image processing techniques that analyses and classify cells for implantation using a grading scheme which is used in clinic for day 2 embryos.

A. Embryo Implantation Problems.

Multiple implantations of embryos will lead to multiple pregnancies, those frequently produced by IVF. They are associated with significantly elevated risks of serious complications. Mothers carrying twins or triplets have an increased incidence of pre-eclampsia, maternal hemorrhage, operative delivery, uterine rupture, and preterm labour. Multiple pregnancies can easily be prevented by transferring fewer embryos to the mother's uterus each cycle, the ideal strategy being single embryo transfer. However, restricting the number of embryos transferred has a negative impact on the likelihood of a patient becoming pregnant each cycle. The reason for this is that the embryos produced in a typical IVF cycle are extremely heterogeneous in terms of their ability to form a viable pregnancy. Transferring a single embryo transfer (SET) is there for eessential but embryo chosen for transfer should be of greatest potential for forming a pregnancy and producing a healthy child.

Different algorithms that were used for segmentation of human embryos, some of them worked on Day 1, 2 or even day 5 embryos, and provided a basis for identifying potentially effective algorithms. Semi-automatic and manual methods were required, so it is likely that algorithms would need to be developed and tuned for the Day 2 as well as Day 3 images. Automatic image analysis may help embryo selection and, consequently, lead to an improvement of the IVF process. Many work concerning automatic image analysis of early stage (days 1 to 2 or 5 post-fertilization) human embryos [1], [2], [3], to the best of our knowledge but still the efficiency remains poor. This is challenging due to varied appearance and quality of images.

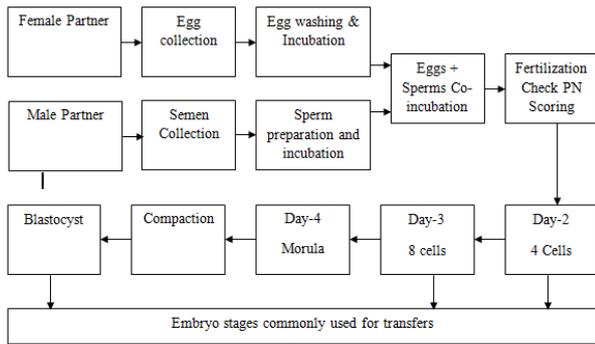


Fig.1: IVF and embryo transfer –procedural Flowchart

II. GRADING OF HUMAN EMBRYOS

In vitro fertilization (IVF) is a process by which female's egg cells are fertilized by sperm outside the body, in vitro. IVF belongs to assisted reproductive technology (ART), which is used in infertility treatments. In IVF procedure, retrieved oocytes are first fertilized and then are cultured for five days as depicted in Fig.2; later embryos will be transferred to the female's uterus. In order to improve the chance of positive pregnancy, these embryos must be inspected and only the good quality embryos with the highest normal growth potential should be transferred. The selection process is done manually and requires experts (such as clinical embryologist) to grade the embryos according to their morphologies and development patterns at different growth stages and ⁵ pronuclear morphology. ⁶

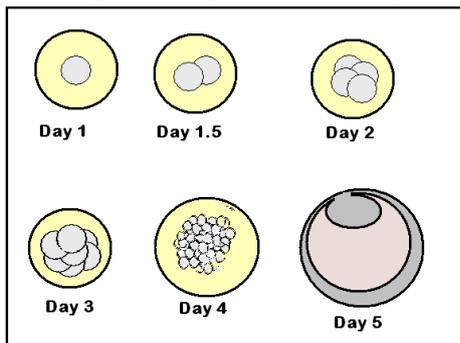


Fig.2: Embryo Development Stages

Unacceptably high rates of three or more embryo transfers in select countries resulting in multiple births and adverse perinatal outcomes⁷.

This makes the IVF embryo selection procedure subjective and becomes very laborious in a center performing high volume (more number of cases). To support this time lapse imaging systems (Embryo scope, Primovision, EscoMiri L) have entered the market but are too expensive. This will be an added burden on the patient and hence cannot be afforded by all the units. Many efforts have been made to identify an efficient and fast method that recognizes quality of the blastomeric from a single embryo without the need of three dimensional image⁸, using blastomere size as biomarker for fragmentation⁹. Solutions that decrease IVF's cost and/or systems that help in embryo scoring are very desirable. We are proposing a research towards an automated embryo grading system which analyzes various aspects of embryos and their growth, particularly at Fertilization (PN

Score), 4cells stage, 8 cells stage and blastocyst stages.

A. Problem characteristics

Since implanting more than one embryo caused multiple pregnancies, it is better for both the mother and the baby to try to minimize the number of embryos. An automated system that is able to achieve this would reduce the load on the IVF screeners and provide a consistent and uniform selection of embryos for implantation. Each clinic chooses a grading system according to many issues, such as the culture media available, the extra cost needed for longer culturing embryos and sometimes the ethical rules of the country or even the religion. The clinic that agreed to support this work was KLE Dr Prabhakar Kore Hospital & MRC this clinic re-implants the embryos on Day 2 or Day 3 based on the subjective analysis, hence uses the Cleaved embryo grading system in particular to choose the embryos. Hence the images used in this study, were Day 2 or Day 3, and their general appearance was the 4 cell embryo or 8 cells seen in Fig.2.

B. Features to be extracted:

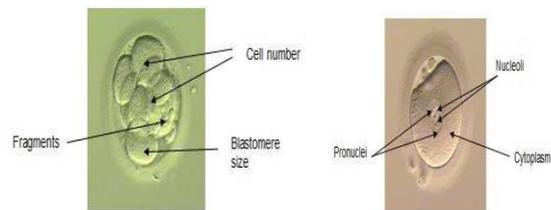


Fig.3: Human Embryo Features

The Embryo features which can be extracted are Nucleoli, Pronuclear, cell number and size of the Blastomeric. Map the characteristics and key features of the Day 2 or Day 3 embryo cells that would make them suitable for implantation into features that can be detected by the system.

- Pre-process the image to compensate for magnification and illumination variations in the microscope images.
- Develop and compare different image segmentation and feature extraction techniques appropriate to these images.
- Identify the most accurate image analysis techniques for classifying the embryo as suitable for implantation.
- Investigate the performance of the approach using images of embryos taken with different microscope magnifications.

Edge detection techniques applied for three different edge-detectors, for pre-processing the image date for the Hough Transform. The Sobel edge-detector gave the poorest results with the lowest matching factors compared to the other two techniques. In the noisy images, the process found false cells with similar matching factors to those of the true cells, and for particularly noisy images, the technique failed to detect true cells and detected false cells with high matching factors. The lowest numbers of false cells that were found was using the 3x3 kernel, although

it detected slightly fewer true cells than for the Sobel edge-detector.

B EMBRYO DETECTION USING BINARY TEMPLATE MATCHING

The Hough Transform and the template matching techniques as discussed may not give the exact extraction of the circle, so an enhanced template matching technique is developed in an attempt to improve on the poor classifications of the embryos.

CONTENTS OF THE TEMPLATE:

Although the template could have contained a disk, whose size corresponds to the size of the blastomeric, it was expected that the matching process would be confused by the overlap of the cells, and so it was decided to design a template with a ring to match the edge of the blastomeric, Fig.4.shows a sample of such a template. The thickness of the ring was created to be similar to the thickness of the cell.



Fig.4: Template

Each image is converted to its binary form after detecting its edges using different edge detection techniques as suggested in the previous report.



Fig.5: Binary image representation

As both the image and template are now in binary form, it is less complex and simpler to perform a simple AND operation between the two arrays and then count the number of matches (1s). In this case, the maximum value indicates the position of the best match. As with the previous techniques, all peaks are found for each image when processed with a particular ring diameter, and the redundant ones are eliminated.

The template can be compared with digital edged images got from edge detection techniques, then moving the template over the image will give us the matches with each image.

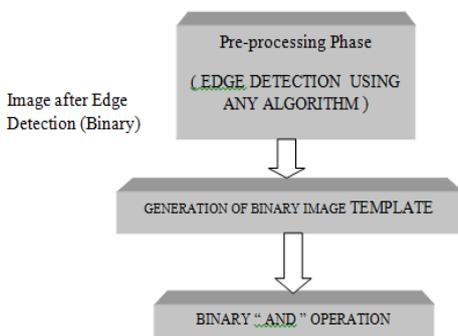


Fig6: Flow Chart of Medical Preprocessing

The above process can be repeated for the set of images obtained from different edge detection algorithms.

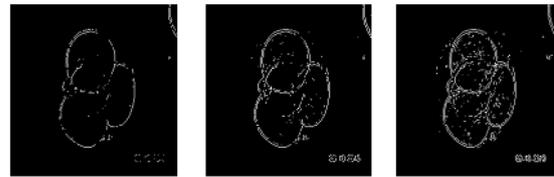


Fig7: Sobel Edge with different thresholds

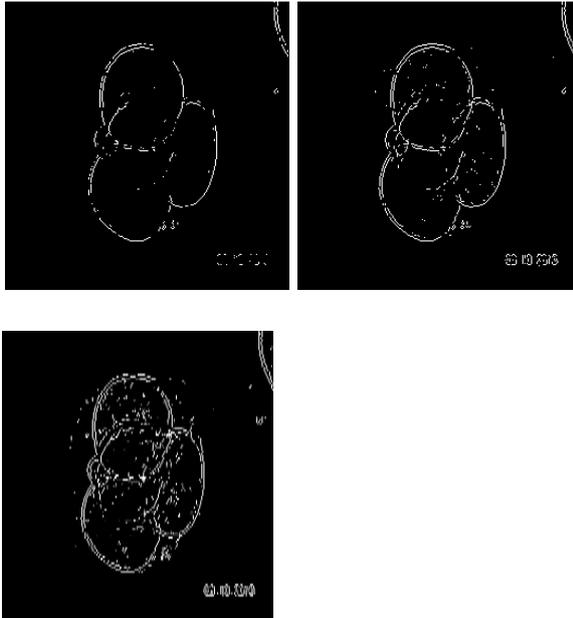
As seen by the above result of edges the Sobel will give a low percentage of enhancements, but by increasing the threshold the clearance of edges can be enhanced. The Canny Edge and Prewitt have given a better edge enhancement comparatively.

Each above edge detection technique suggested will manage to find cells that are almost a circle and matching can be obtained. There are also cells which have to be detected in the background, the similarity percentage in this case may be higher, but unfortunately some of those can be false cells which are missing in the above algorithm.

Table 1: Number of count cell detected

Digital Images Preprocessed (Edge detection techniques)	Total Number of cells detected	Potential cell detected		False cells detected
		count	%	
	94	08	70	86
	94	07	69	88
	94	06	60	84
	87	05	50	74

Here we intend to implement several other cell detection algorithms and compare their performance in their ability to detect true cells. This stage will be considered as a pre-processing stage for a classification algorithm that can suggest success rate of implanting a given embryo. These classification algorithms will be soft computing algorithms like Artificial Neural Networks (ANNs). Currently, there are many types of ANNs available for such classification work. Suitability of specific type of ANN has to be studied.



III DISCUSSIONS & FUTURE WORK

The primary objective of the study is to develop automated embryo grading system replacing a manual embryo grading by an embryologist. This can minimize interpersonal errors in grading and hence maintaining uniformity in the laboratory outcome. This ultimately lowers the overall cost associated with the time lapsed imaging systems. Automated morphological evaluation is likely to save the embryology staff a significant amount of time. Hence the efficiency of identifying the potential embryo for implantation may become easier which will ease the job of embryologists.

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