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# Predicting pregnancy rate following multiple embryo transfers using algorithms developed through static image analysis

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**KEY MESSAGE**
We propose an innovative method to use all embryo images from a transfer cycle as one unit to predict pregnancy rate. This will help embryologists select embryos with high implantation potential.

A B S T R A C T

Single-embryo image assessment involves a high degree of inaccuracy because of the imprecise labelling of the transferred embryo images. In this study, we considered the entire transfer cycle to predict the implantation potential of embryos, and propose a novel algorithm based on a combination of local binary pattern texture feature and Adaboost classifiers to predict pregnancy rate. The first step of the proposed method was to extract the features of the embryo images using the local binary pattern operator. After this, multiple embryo images in a transfer cycle were considered as one entity, and the pregnancy rate was predicted using three classifiers: the Real Adaboost, Gentle Adaboost, and Modest Adaboost. Finally, the pregnancy rate was determined via the majority vote rule based on classification results of the three Adaboost classifiers. The proposed algorithm was verified to have a good predictive performance and may assist the embryologist and clinician to select embryos to transfer and in turn improve pregnancy rate.


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## Introduction

According to a survey by the China Population Association in 2012, the incidence of infertility and sterility in China had increased to 12.5% among women of childbearing age compared with only 3% 20 years ago (Xinhua/China Daily, 2012). Currently, IVF and embryo transfer (IVF–ET) is one of the primary methods for treating infertility. Although IVF–ET technology has considerably improved over the past 30 years, its efficacy remains relatively low; the success rate of IVF–ET is less than 30% (Dyer et al., 2016). To increase the success rate of this procedure, embryologists often transfer multiple embryos to the uterus in each cycle, although this may increase the occurrence of multiple pregnancies (Filho et al., 2010; Ubaldi et al., 2015). The primary reason for transferring multiple embryos is the unavailability of an accurate and reliable method for selecting high-quality embryos. Usually, selection of embryos is based on the embryologist's experience in observing the morphological features of embryo images along with clinical data. This method is widely used in clinical practice; however, this technique provides only a rough estimate of implantation potential of embryos. Moreover, the process is highly subjective considering the individual differences between embryologists (Conaghan et al., 2013; Paternot et al., 2013), and it is challenging to predict whether the procedure will result in a pregnancy. This study, therefore, aimed to improve the interpretation of embryo images based on whole transfer cycles in order to predict pregnancy rate more accurately. The proposed algorithm can assist the embryologist and clinician to choose embryos for transfer and in turn improve pregnancy rate.

Previous studies mainly focused on evaluating the potential of a single embryo transfer based on the decision support system in which embryologists select embryos with highest potential (Aiduk and Zernicka-Goetz, 2012; Balaban and Urman, 2006a; Baxter Bendus et al., 2006; Borini et al., 2005; Conaghan et al., 2013). According to the different stages of embryo development, several algorithms are avaialble for embryo quality assessment. For cleavage stage embryos (Gabrielsen et al., 2000; Hesters et al., 2008; Tian et al., 2014), evaluation systems are primarily based on several factors, including fragmentation rate, presence of mononucleated blastomeres, number and size of nuclei, thickness of the zona pellucida and number and symmetry of blastomeres. For blastocyst stage embryos (Balaban et al., 2006b; Gardner et al., 2004; Papanikolaou et al., 2006), the degree of expansion of the blastocyst cavity, the inner cell mass and the number and cohesion of trophectoderm cells are the main considerations. These methods predominantly rely on simple analysis of the morphological characteristics of embryos during each specific stage, in which case embryos are roughly divided into several levels of quality for embryo transfer. The developmental potential of an embryo, however, is not completely related to its morphological characteristics. In order to decrease the embryologist's subjectivity and improve the success rates of embryo transfer, some novel methods, such as time-lapse techniques and pre-implantation genetic screening, are being increasingly used in clinical applications (Kovacs, 2014; Lagalla et al., 2015; Machtinger and Racowsky, 2013). These new technologies, however, are not commonly used, especially in developing countries.

With increased application of IVF–ET technology in practice, some researchers have begun to use computers to analyse human embryo images (Manna et al., 2013; Mölder et al., 2015; Patrizi et al., 2004; Wang et al., 2013) and predict embryo implantation potential. These automated approaches can be roughly divided into two categories: assessment of embryo implantation potential based on a single embryo image (van Loendersloot et al., 2014; Wong et al., 2013) and prediction of pregnancy rate based on the whole transfer cycle (Grimmett and Stirzaker, 2009; Ojala et al., 1996). With some automated systems, it is difficult to assess the implantation potential of a single embryo, because the 'quality label' is assigned to all transferred embryos and not to each individual embryo. For example, of several embryos in a successful transfer cycle, the particular embryos that implanted successfully are unknown. Therefore, in training a classifier, it seems impossible to accurately label all embryo images, which may result in inaccuracy of classifiers. Moreover, small differences in features between positive and negative samples, and the large difference in numbers between the two training sample types, would further weaken classifier performance. Prediction of pregnancy rate based on the whole transfer cycle considers several embryos in one transfer cycle as a whole, which precludes problems associated with uncertain category labels. Saith et al. (1998) used the probability tree model of C4.5 algorithm to express the feature relationship of the two classes, and only considered four out of 53 features to be predictive. The four features considered included embryo grade, cell number, follicle size, and follicular fluid volume. Morales et al. (2008a) proposed an algorithm based on the Bayesian classifier to analyse embryo morphology variables and clinical data.

In the present study, a novel algorithm based on pattern recognition technology is proposed for predicting the implantation potential of embryos. The algorithm combines the local binary pattern (LBP) (Manna et al., 2013; Ojala et al., 1996; Yin et al., 2013) and the Adaboost classifiers (Morales et al., 2008b), and considers all embryo images from a transfer cycle as one unit to predict pregnancy rate. The first step of the proposed method was to extract the features of the embryo images using the LBP operator. Subsequently, all LBP features of the embryo images in a transfer cycle were combined into a feature vector, and pregnancy rate was predicted using three classifiers as follows: the Real Adaboost (RA), Gentle Adaboost (GA), and Modest Adaboost (MA). Finally, pregnancy rate was determined via the majority-vote rule based on classification results of the three classifiers.

## Materials and methods

### *Research design*

The experiments were carried out on a data set comprising 931 images from 423 transfer cycles of eligible patients. These patients included all consecutive women aged between 25 and 40 years undergoing their IVF or intracytoplasmic sperm injection (ICSI) cycle, who were to undergo a fresh embryo transfer cycle. Eligible patients were those treated with a conventional starting gonadotrophin dose of 150–225 IU recombinant FSH in a fixed gonadotrophin-releasing hormone (GnRH) agonist protocol (Decapeptyl, 0.1 mg, Ferring). Patients were excluded if they were to undergo natural cycle IVF–ICSI, because, in such cases, no ovarian stimulation was used. Women whose cycles were cancelled, or with no oocyte, retrieved were also excluded from the analysis. The images were obtained from an inverted microscope (TE2000; Nikon) equipped with a video camera (JVC TK-C1481BEC) at a magnification of 200X just before transfer, and managed by an experienced embryologist.

The research was conducted at the Assisted Reproductive Medical Center of Navy General Hospital, China, and involved 423 couples



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