Blastocyst “pumping" is a detrimental feature predicting implantation failure: highly accurate assessment by computer vision analysis of time-lapse videos

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INTRODUCTION

Blastocyst collapse and re-expansion, otherwise known as “blastocyst pumping,” is often observed in vitro during the process of blastulation[1]. Blastocyst “pumping” and its effects on viability and implantation potential has been the subject of numerous studies[1-3].

It is now possible to accurately measure the phenomena of blastocyst pumping in embryo time-lapse (TLS) video frames using computer vision.

We hypothesize that highly accurate computer measurements of developing embryos, using computer vision analyses of time-lapse video sequences, may determine the significance of pumping on implantation rates after embryo transfer.

OBJECTIVE

To evaluate the association between blastocyst pumping, defined as a blastocoelic contraction by more than 8 microns in diameter, and poor implantation rates, independent of other morphokinetic parameters.

The clinical impact of computer vision-based pumping detection is significant. Standard embryo scoring schemes are limited, since they rely on classifying embryos by morphological features that are visible to the human eye[4]. An objective, highly accurate computer vision-based algorithm that automatically quantifies blastocyst pumping behavior may optimize blastocyst selection prior to embryo transfer.

An example of this is shown in the figures below. **Figure 1:** A time-lapse image frame of a Grade AA embryo, as scored by an embryologist, is depicted. Based on its highly-scored morphological features alone, this embryo would have been selected for embryo transfer. **Figure 2**: Two consecutive time-lapse sequence frames of the same Grade AA embryo, captured by TLS 29 hours prior to Figure 1. Our computer vision-based algorithm detected a “minor pumping event” (a diameter of change of ~8 microns, which cannot be seen by the human eye) between the two frames. Based on computer vision analysis, this embryo would be de-selected for embryo transfer.

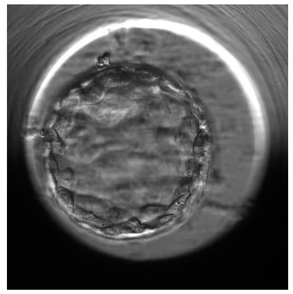

Figure 1: time-lapse image frame of an AA blastocyst

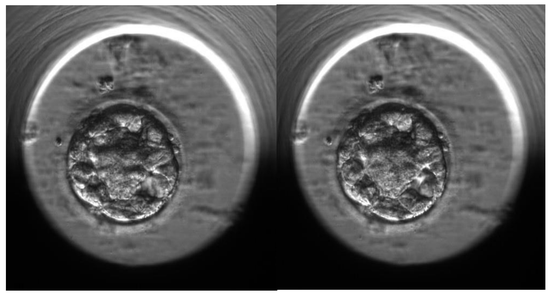

Figure 2: Two consecutive time-lapse sequence frames of the AA blastocyst, captured 29 hours earlier. A “minor pumping event” was automatically detected between the two frames using computer vision-based software.

MATERIALS AND METHODS

We investigated a retrospective cohort of 317 Day 5 expanded blastocysts chosen for transfer, with known implantation data, and 148,441 accompanying time-lapse images.

Since developing blastocysts are rarely uniformly spherical, a fitting algorithm was used as a proxy for blastocyst size in order to quantify changes in blastocyst diameter. We then precisely measured blastocyst diameter, approximated to a best fit circle, in steps of 8 microns.

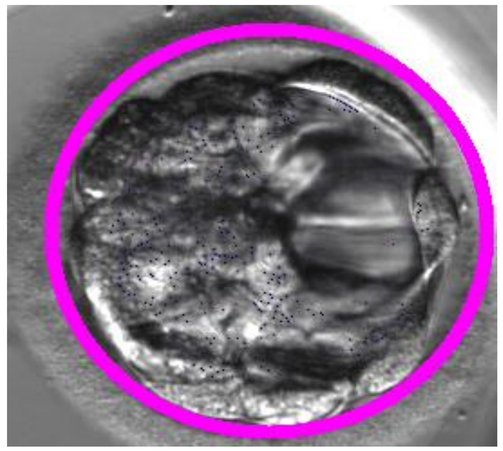

Figure 2: Illustrative time-lapse frame shows the best-circle fitting algorithm used to approximate blastocyst size.

We defined a "pumping event" when the blastocyst diameter was at least 8 microns smaller in an image compared to an image taken 40 minutes earlier.

A “major pumping event” was defined as any case where the blastocyst diameter was at least 16 microns smaller in an image than in the image 40 minutes earlier.

A “minor pumping event” was defined as any case where the blastocyst diameter was at least 8 microns greater, but at least 16 microns smaller in an image compared to an image taken 40 minutes earlier.

An “early pumping event” was defined when the diameter of the blastocyst was less tthan 140 microns.

A “late pumping event” was defined when the diameter of the blastocyst was more than 140 microns.

The extent, number of pumping events and the stage of blastulation at which it occurred were calculated and compared to the embryos’ known implantation outcomes.

RESULTS

- Of the 317 blastocysts, 188 (59.3%) successfully implanted.
- Of the 188 blastocysts that implanted, early pumping was noted in 27 (14%) blastocysts, for a total of 73 events, at average ± SD 110.7±4.2 hours.
- Early pumping events occurred in 22 (17%) of the 129 blastocysts that failed to implant with overall 80 events at average ± SD 112.0±4.8 hours.
- Major pumping events occurred 25 times in 14 (7%) blastocysts that implanted at average ± SD 110.5±7.7 hours vs. 38 events in 18 (14%) blastocysts that failed to implant, at average ± SD 111.7±4.6 hours.
- Major pumping events were significantly correlated with implantation failure (OR 1.87, P=0.03, for at least one major pumping event, OR 2.42, P=0.04 for at least two major pumping events).
- Multiple early pumping events significantly correlated with implantation failure (OR 2.07, P=0.02, for at least three early pumping events, OR 2.55, P=0.02, for at least four early pumping events).

CONCLUSIONS

The computer vision algorithm can accurately quantify changes in blastocyst diameter with an unprecedented accuracy of 8 microns. Multiple "early" or "major" pumping events were found to be uncommon, but when they do occur, they were found to have a high negative predictive value for blastocyst implantation.

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