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## INVITED COMMENTARY

Male Health

### Commentary on the development of a new tool for embryologists to detect testicular sperm cells

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To get higher standards in medical analysis with numerous quality controls and because of the growth of industrialization in the laboratories, automation became necessary and is now well established. In andrology laboratories, sperm analysis remains a challenge for automation and progress is slower than in other fields of medical laboratories. First, because of specific sperm cells that are fast-moving cells in different directions, this analysis was certainly difficult to be digitized. Another possible reason is that it has been neglected considering its low volume of analysis compared to the other routine blood analysis. Nonetheless, the first Computer Aided Sperm Analysis (CASA) machines have been developed since 1986 and it took years before considering their results suitable. The first studies with such machines were mainly used for research purpose and helped us understand the very particular movement of the spermatozoa. For example, unique states such as hyperactivation, which is required for fertilization, were characterized.<sup>1</sup>

Nowadays, CASA systems appear as more reliable and fulfill the required quality controls in an easier and more reproducible way.<sup>2</sup> Hence, more and more andrology laboratories are considering their purchase although they do not cover the whole range of sperm count, in particular, for the low and very low sperm count. For example, azoospermia diagnosis still needs a manual analysis. In those cases, testicular biopsy is still the ultimate test to ascertain the presence or absence of sperm production. In obstructive azoospermia, numerous spermatozoa can be found in the epididymis and the testis upstream of the obstruction. In nonobstructive azoospermia, manual seeking of sperm cells under the microscope can be a tedious challenge for an embryologist and the results will greatly change the patient's reproductive perspective.

Due to the good results obtained with frozen/thawed sperm, asynchronous testicular biopsies are performed in many laboratories. Hence, when no spermatozoa could be found, unnecessary oocyte hyperstimulation is avoided. When sperm cells are observed with at least a few motile, testicular cells including spermatozoa are frozen to be used in a second time. Later, the day of the intracytoplasmic sperm injection (ICSI) procedure, testicular sperm cells are thawed, and in some difficult case with very few spermatozoa, it can take several hours in order to find the correct sperm to be injected into the oocyte. The motility of the spermatozoa, sometimes twitching sperm, is paramount to testify its viability. In rare cases, all spermatozoa are immotile and specific viability tests are needed for each.

The aim of the study by Wu *et al.*<sup>3</sup> is to develop a new CASA system dedicated to search sperm cells in testicular cell suspension. It is suggested that the camera and the specific software will help the embryologist by focusing faster on the fields where sperm cells are present. Then, the

embryologist can decide if it can be used for fertilization when it is motile and (sub)normal. Major challenges were resolved; the testicular tissue is known to contain barely any complete mature spermatozoa as the final maturity step is assumed to take place in the epididymis. In normal physiology, most of them should have at least cytoplasmic residue with a complete flagellum in the testis, but other abnormal morphologies should also be detected at this point. Hence, the software had had to include such variations of the sperm morphology. And, after a specific dilution to assure even distribution, it seems to well detect such sperm cells from many other kinds of cells present in this tissue.

This study is a proof of concept of this technology in detecting testicular sperm cells in a suspension, and it appears to do so faster than the human eye. The speed is also a key point as the several hours sometimes needed can be detrimental for the sperm cells, the oocyte, and the ICSI results. However, the relevance and the help this model can bring to the embryologists have to be shown, as this preliminary study relies solely on static images. We all know how pictures are somehow far from what can be observed under our inverted microscopes. Detecting moving cells, even at a slow motion in those cases, may indeed be a challenge for the software and has not been evaluated. The depth of the cell suspension is also a matter of concern that has not been studied here on images, but usually after preparation, most of the cells remain in narrow field.

This study opens a new field in the CASA system for testicular sperm cell suspension which contains many different types of cells including mature and immature spermatozoa. The accuracy of the human eye appears still superior, but what is expected here is a tool to quickly detect sperm cells which will be selected or not by the embryologist. Then, the ICSI procedure should be performed more rapidly and this also counts for its success rate.<sup>4</sup> There is no doubt that further versions will also help the embryologists to select the best sperm by its morphology. However, for now, the real place and efficiency of this new CASA system in a laboratory setup must be shown before further developments.

#### COMPETING INTERESTS

Both authors declare no competing interests.

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