

## Sperm Vacuoles and Reproductive Outcome

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### Editorial

It is estimated that the male factor contributes to half of the infertility in couples attending for assisted reproductive techniques (ART). Therefore the semen analysis remains the starting point to evaluate main causes of infertility and in case of oligospermic semen the assessment of sperm morphology may help to choose the best spermatozoon to use for the intracytoplasmic sperm injection (ICSI).

In order to select the ideal spermatozoon and enhance the chance of pregnancy, in recent years most of the IVF centers have started to perform MSOME, i.e., the motile sperm organelle morphology examination followed by IMSI, the intracytoplasmic morphologically selected sperm injection in the oocytes [1].

Clinical significance of sperm anomalies is a matter of debate. Many studies demonstrate that an accurate evaluation of sperm anomalies plays a crucial role in determining the male fertility potential and the decision for the treatment of patients in IVF programs [2].

However contrasting data show that bad sperm morphology is a parameter differently associated to the chance of pregnancy outcome [3-6].

By examining organelles at the high MSOME magnification (>5000 X), a special attention was paid on the vacuoles in the sperm head. These appear to be small malformations considered to be an alteration of the sperm cell structure and believed to exert an adverse impact on the following embryo development. At the optical microscope, vacuoles appear as small holes, but ultrastructural studies showed that they are abnormal nuclear concavities covered by the acrosome and the plasma and acrosomal membranes [7] (Figure 1).



**Figure 1:** Representative image of a human sperm population showing normal morphology >4% and 60% of differently vacuolated heads. Magnification 1000X.

Some studies describe a nuclear origin and account for a pathological role of vacuoles [8] starting from previous findings that higher percentage of vacuoles was reported in sperm head of infertile men [9]. Following studies reported that vacuoles exert a negative impact on the sperm functionality associating them with either DNA fragmentation [10] or an impaired DNA packaging and failure of chromatin condensation [7,11,12]. These hypotheses were supported by clinical studies that correlated sperm vacuoles to a decrease in the fertilization rate and failed pregnancies, further encouraging the application of MSOME, as a tool that may enhance the ART success and even proposing a cut off value for vacuoles estimation [13,14].

In this line, in IVF centers the use of IMSI has been increased in order to exclude the injection of sperm bearing vacuoles especially in cases of couples who experienced recurrent implantation failures and pregnancy loss [15,16].

Contrasting data are more recently revising the pathological role of vacuoles. Starting from the observations that a significant decrease of vacuole numbers was found following acrosome reaction [17,18]. It was hypothesized an acrosomal origin and a physiological role of these organelles [19].

The fact that MSOME had no impact on early embryo development [20], and that no correlation was found between vacuoles, sperm DNA packaging and structure, corroborated the idea that vacuoles are not negative parameters and therefore should be not used as a predictive factor of sperm quality. On the other hand it has also been claimed that IMSI is time consuming technique that may also induce oocyte aging as an additional disadvantage [21,22]. In support of this new scenario it is speculated that vacuoles are pre-existing structures and that cannot be modified by environmental conditions [23-25]. In our recent study [26] we have shown that vacuoles in sperm head are not related to abnormal head morphology and do not affect live birth rate, confirming previous findings that vacuoles are physiological features not altering sperm functionality.

### Conclusion

It is well known the paternal effect that influences embryo development since a poor sperm quality may lead to poor blastocyst formation [27-29].

It is clear that whatever technique leads to ameliorate fertilization success and pregnancy outcome is worth to be applied in the IVF routine practice. This was the case of IMSI that providing a deep evaluation of

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the fine sperm morphology was included in the treatments of infertile couples; nonetheless contrasting data exist in literature on the real advantages of using IMSI to increase the pregnancy rate.

At present, major question addresses if the presence of vacuoles in the sperm heads may be considered a diagnostic tool to explain idiopathic infertility [23].

Due to different clinical results reported in above mentioned studies, the pros and cons of potential interaction between sperm vacuoles occurrence and fertilization success deserve further investigations and statistical support in order to render ART techniques effective and safe at the same time.

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