

# SVE

International Society for In Vitro Fertilization

Webinar -Special interest group EMBRYOLOGY

Date: Time: time	7 <sup>th</sup> of October 7pm, Japanese standard	All about PIEZO-ICSI	
Venue:	the "Zoom" auditorium maximum	$\Rightarrow$	Safe operations
Registered: Participated: Background:	329 professionals 118 professionals mostly embryologists and medical doctors	$\Rightarrow$	Standard procedures
		$\Rightarrow$	Improved results
Countries:	from Japan, Malaysia, Korea,		

Session Chair: Dr. Tetsunori Mukaida





Mexico, Thailand, New Zealand, UK, US, Poland, Hungary, Israel, Korea,

mention some

Norway, India, UAE, Norway, Germany, Spain, Argentina, Turkey, Romania, Jordan, Greece, China, .. just to

Dr. Tetsunori Mukaida medial director Hiroshima HART Clinic - Japan



Dr. Csaba Pribenszky assoc. prof. University of Veterinary Medicine, Budapest, Hungary



Dr. Kenichiro Hiraoka laboratory director Kameda Medical Center -Japan



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### **Topics and summary**

The three presentations by the three professionals have addressed the integration of the piezo technique into the process of ICSI, from three different angles.

Dr. Hiraoka, who can absolutely be credited with fine-tuning the piezo technique, has focused mostly onto the technicalities in great detail. Dr. Pribenszky has discussed the results of their current metanalysis comparing the results achieved by conventional or piezo-ICSI. He also presented the development and first clinical results of a new, medical operating liquid for piezo-ICSI. Finally, Dr. Mukaida, who also chaired the session, has presented excessive clinical data how piezo-ICSI functions in the routine of a busy IVF clinic, who turned 100 % piezo five years ago.

Besides the tight focus of the three presentations there were quite a few overlaps regarding technicalities and clinical benefits, which explained the basic concept well. The talks were in nice harmony, showing well-structured historical, basic and practical information for the professionals who are just getting to know ICSI as well as deep, analytic detailed information for those who already use it in practice.



SIG Embryology - PIEZO ICSI as a next assisted fertilization technology Date: 7<sup>th</sup> October 2022, 19:00 – 19:25 (JST)

## PIEZO ICSI setting and its utilization in ART Laboratory

### Kenichiro Hiraoka Ph.D

Kameda Medical Center Kameda IVF Clinic Makuhari Tokyo Medical and Dental University

Dr. Hiraoka started with describing conventional ICSI, highlighting that the micropipette affects with positive pressure that deforms the cytoplasm of the oocyte. This increased cytoplasmic pressure may lead to the damage of the cytoskeleton. Also, in order to break the oolemma of the oocyte, cytoplasm aspiration of is necessary even with sharp.

spiked micropipette. Each egg differs in the hardness of the zona pellucida and the elasticity of oolemma. Those differences require meticulous, professional skills from the embryologists to judge and adjust the proper performance of conventional ICSI procedures. It requires a long learning curve to master the technique of conventional ICSI and may create variable results of fertilization and oocyte degeneration. Piezo-ICSI, on the other hand, may be the add-on that solves all the problems described above.

The detailed mechanism of piezo pulse was also described and the settings affecting the piezo effect were shown. The Kameda Clinic could maximize fertilization rates and minimize oocyte degradation rates after introducing piezo-ICSI for all patients.



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Another important point that was the introduction of piezo has significantly shortened learning curve for mastering ICSI, to about a 2-3 months period, instead of > 1 year required to perform proper conventional ICSI. Dr. Hiraoka's conclusion was that piezo-ICSI makes it significantly easier to master ICSI for embryologists and it



#### **PIEZO-ICSI** setting



creates steady clinical results that may even be better compared to that of conventional ICSI.



Dr. Pribenszky's main focus was the new, medical operating liquid for piezo ICSI that enables the safe use of the technique in a human clinical setup.

The idea of using piezo or other electro-mechanic effect to aid the microinjection procedures is not new, the first publications date back to the beginning of the 80's. The

technology has been picked up by a lot of clinics in Japan and is of wider interest with the promise of standardizing the ICSI technique and improving normal fertilization rates especially in the age group above 37. The technology requires a flat-tipped injecting micropipette and a special operating liquid that is backfilled into the micropipette and is in direct contact with the media holding the sperm. It is the operating liquid which is the last barrier for safe operations.

The introduction of Fluorinert and later Novec (both manufactured by 3M) to replace mercury as an operating liquid was an important move that helped piezo-ICSI to spread amongst human IVF labs. However, none of the these currently used operating liquids are made for medical operations. They are industrial heat transfer fluids, mixtures of inert substances and toxic byproducts. Their common features are low viscosity, high density, very low or no solubility in water, a slight - moderate cytotoxicity in case of direct contact with cells and slight environmental toxicity. For the safe operations in human IVF, there is a need for a chemically and biologically inert, defined operating liquid. Fully fluorinated carbons (perfluorocarbons) contain only carbon and fluorine. As a molecule, they are inert, with favorable physical properties for piezo ICSI.



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Many substances have been tested to come up with an alternative to the current industrial chemicals. Amongst many, perfluoro-n-octane (PFNO) proved to be the most effective for piezo ICSI, although under-fluorinated toxic compounds are essentially created during production of perfluoro octanes, even at PFNO. Impurities, like acids, C-H compounds, fluorinated alcohols, and

others altogether the cause of the cytotoxicity and they are all present in the currently used OLs. and even in commercially available PFNO. For this reason, industrial PFNO has further been processed and purified by a proprietary method turning it into a pure, truly singlemolecule medical product. This purified PFNO is insoluble in water and proved to be



absolutely inert, not effecting at all embryo development even in case of long-term direct contact. First clinical results with the new, medical PFNO operating liquid were published in RBM Online in 2021 (by Zander-Fox et al., from the Monash IVF group in Australia). Authors found that PIEZO accounted for significantly increased fertilization rates (80.6% vs. 65.9%, p<0.05), significantly decreased oocyte degeneration rates (3.8% vs. 10.2%, p<0.05), significantly lower abnormal fertilization rates and more good quality embryos for transfer or cryopreservation. Dr. Pribenszky has concluded, that piezo ICSI, used with medical operating liquid has become a safe and defined medical procedure, all the way.

# **ISIVF** Webinar 2022

'Piezo ICSI with intracytoplasmic spindle confirmation as an ultimate ICSI approach leads to improved clinical performance at the era of PGT-A

Tetsunori MUKAIDA, M.D. Director of *Hiroshima HART Clinic* 

Dr. Mukaida presented his clinical experience of piezo ICSI, including the reason why his clinic has decided to change the conventional ICSI procedures to piezo ICSI completely. Since conventional ICSI was reported for the case of severe male factor infertility to overcome fertilization failures due to low sperm count and/or low motility, more than three decades have passed without any dramatic change in the procedure itself. As described above,



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conventional ICSI with sharp, spike-tipped micropipette may require high level of technical skills and experience to puncture the oolemma with the aspiration of the cytoplasm. It takes usually one to two years to master conventional ICSI after going through the training process.

However, it usually takes only two to three months to master the piezo ICSI technique. Because the continuous piezo pulse-series makes the zona penetration flowless, without any deformity of the oocyte and single piezo pulse achieves proper oolemma breakage without any aspiration of cytoplasm the depositing of the sperm in the cytoplasm of oocyte is quite straightforward. Dr. Mukaida's introduced piezo ICSI approach, it just took s 4 to 6 months to master this technique for all of the embryologists. Since



then, HART clinic changed the way how ICSI is performed. ICSI to piezo ICSI, fertilization rate was increased (69% to 78% at all age group) and degeneration rate was decreased (8,3% to 2.8% at all age group). Consequence of those improvement created more available embryos for culture and more blastocysts for cryopreservation.

The organizers thank the audience the very active participation and the series of questions during and at the end of the presentations.