PI-PICSI-ROW • Rev. A • 09/2020

CooperSurgical

PICSI® Dish

Sperm Selection Device

CE 2797

DEVICE DESCRIPTION

The PICSI® Sperm Selection Device is a polystyrene culture dish with three microdots of hyaluronan attached to the interior bottom. Three locating lines embossed on the bottom exterior of the dish facilitate the location of the microdots. The microdot is found in an area approximately 2 mm wide and 3 mm long projecting from the end of the locating line. The device is sterile, Sterility Assurance Level 10-6, essentially free of endotoxin and non-toxic to embryos.

The results of each batch are stated on a Certificate of Analysis, which is available at fertility.coopersurgical.com.

WARNING

U.S. Federal law restricts this device to the sale by, or on the order of, a physician.

INTENDED USE

In the treatment of infertile couples by Intracytoplasmic Sperm Injection (ICSI), the PICSI® Sperm Selection Device is indicated for the selection of mature sperm for injection.

PRINCIPLE OF THE DEVICE

Hyaluronan is a main component of the cumulus oophorus matrix that surrounds the oocyte. The head of a mature sperm carries a hyaluronan-specific receptor that enables mature sperm to bind to hyaluronan (1). In contrast, immature sperm do not bind. Mature sperm exhibit a high DNA chain integrity (2), a normal frequency of chromosomal aneuploidies and provide a paternal contribution to the zygote comparable to that of sperm selected by the zona pellucida during natural fertilization (3).

In the usual practice of ICSI, sperm are visually selected for injection on the basis of their morphology and motility. However, this approach does not reflect the genomic integrity of the sperm and its ability to provide the best paternal contribution to the zygote. The PICSI® Sperm Selection Device provides a means to select mature sperm based on their ability to bind to hyaluronan hydrogel. The PICSI® Sperm Selection Device mimics the natural binding of mature sperm to the cumulus oophorous, an important selective step in natural fertilization.

PREPARATION FOR USE:

Hydrate the hyaluronan microdots by placing single 10-µL droplets of Human Tubal Fluid (HTF) containing at least 5 mg/mL serum protein or other suitable sperm diluent at the end of each locating line covering the area where the microdot is situated (Figure 1). Alternatively, the sperm suspension can be added directly to the dry microdot. Drops of Polyvinylpyrrolidone (PVP) or other fluids useful for manipulating sperm may also be placed elsewhere on the dish at this time. Carefully flood the dish with tissue culture oil to prepare it for use. Hydrating the microdot before applying the sperm gives the hyaluronan time to swell. Swelling and sperm binding begin normally in 5 minutes or less. However some microdots may require 30 minutes or more to reach full binding capability. Therefore, whenever marginal sperm binding is observed, pre-hydrate for 30 minutes or more, or allow sperm to incubate on the dot for 30 minutes or more before selecting sperm.

INSTRUCTIONS FOR USE

Add the sperm to the pre-hydrated microdot in a volume equal to or greater than that used to pre-hydrate the dot (approximately 10 µL). Touch the tip of the micropipette containing the sperm to the edge of the hydrating drop at the bottom of the dish under the oil and expel the sperm. By delivering the sperm in a volume equal to the hydrating fluid, immediate mixing and delivery of sperm to the vicinity of the microdot is assured. If the sperm are delivered in a smaller volume at the edge of the drop, greater than 30 minutes may be required for them to swim through the hydrating fluid to the microdot. Once bound, hyaluronan-bound sperm are easily identified: they exhibit no progressive migration despite vigorous tail beating.

Factors governing sperm binding

To rapidly populate the microdot with bound sperm, place approximately 100,000 hyaluronan-binding sperm per mL (approximately 1,000-2,000 total sperm in 10-20 µL volume) over the microdot, see Figure 2. As time passes, the number of bound sperm will increase as more swimming sperm make contact with the hyaluronan microdot.

Sperm Location Selection

The wall of the hyaluronan microdot is a physical barrier to which many sperm will bind since this is usually the first point of contact. It is sometimes difficult to distinguish whether the sperm are bound or they are simply swimming against the edge of the microdot. You may be sure of selecting bound sperm by selecting them from the interior of the microdot.

Obtaining a good density of bound sperm

If the density of bound sperm is too high or too low for good sperm selection, dilute or concentrate the prepared sperm sample and use the adjusted sperm sample to seed the next microdot. Three microdots are provided on each PICSI® Sperm Selection Device to give a sufficient opportunity.

Sperm collection

To collect a bound sperm, position the tip of the ICSI micropipette next to the sperm and gently suck fluid into the pipette, drawing in the sperm. Continue collecting until 20-50 sperm are captured. Expel the captured sperm into a PVP drop to process them for ICSI (inactivating the tail, re-evaluating motility and morphology.) From the PVP droplet, select and load single, processed sperm for injection into the oocytes according to your standard injection protocol.

Temperature

Sperm bind best to hyaluronan hydrogel at temperatures below 30°C. At temperatures above 30°C, sperm swimming vigor increases and the swimming force may overcome the binding force. The result is that about one-third of sperm bound at room temperature will show some progressive migration at 37°C and may be deemed not bound, immature. PICSI® Sperm Selection Device dishes placed on a 37°C heated stage will come to about 33°C and then remain at that temperature. At 33°C or even at 37°C, many bound sperm will remain available for selection.

TECHNIQUE CONSIDERATIONS

Microdot shape

The PICSI® Sperm Selection Device hyaluronan microdot is crater-shaped. The edge of the microdot is a raised wall of hydrogel surrounding a low, flat interior layer. The wall is flexible and may be irregular in shape due to uneven hydration of the hydrogel.

The hydrogel wall can be pierced and torn by an ICSI micropipette driven directly into it. It is best to position the elevated micropipette tip over the microdot interior and lower it to the microdot surface for recovery of sperm.

Microdot caves

During manufacture, uneven hydration may cause segments of the microdot wall to create small “caves” that open toward the inside edge of the wall. Sperm that swim into a cave are trapped, not bound. Trapped sperm usually all face away from the center of the microdot and show vigorously beating tails, often in clusters. The heads of trapped sperm can move laterally and sometimes back and forth within the walls of the cave. Trapped sperm should not be selected since their binding status is unclear.

Microdot stability

If a part of the wall separates from the polystyrene, the same forces that create caves can cause the microdot wall to progressively detach from the dish and coil up like a spring. When this occurs, some or all of the wall will separate from the microdot. However, the microdot interior hyaluronan layer will remain intact. The interior hyaluronan layer is stable for hours, it collects and houses bound sperm that may be used for ICSI. Sperm bound to the curled up wall remnant should not be used for sperm selection and isolation.

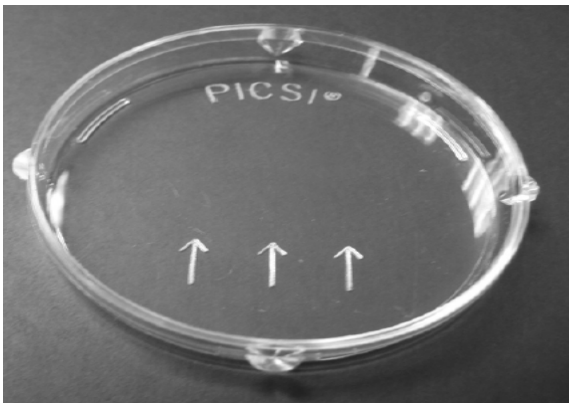
Troubleshooting

If sperm do not bind to the microdot:

1. Determine that the sperm sample contains mature, hyaluronan-binding sperm by assaying with an HBA® Hyaluronan Binding Assay. If the HBA score is near zero (<5%), no sperm binding is expected (In some laboratories, as much as 10% of the donor sperm population shows no sperm binding. This is a significant factor contributing to infertility).
2. How long have the sperm been incubated on the microdot? Binding is directly related to the time allowed for binding. Sperm bind when they make contact with the hyaluronan microdot, swimming randomly. The number of sperm bound to the dot will grow with time as more sperm encounter the hyaluronan microdot. Check the microdot periodically over two hours to see if sufficient bound sperm have accumulated for an ICSI procedure.
3. The density of hyaluronan-binding sperm is critical. Rapid population of the microdot requires a density of at least 100,000 hyaluronan-binding sperm per mL. If the HBA score is low, the total sperm density must be increased to deliver an effective number of hyaluronan-binding sperm. For example: if the HBA score is 10%, 1,000,000 total sperm per mL will be required to deliver 100,000 hyaluronan-binding sperm per mL.

Figure 1

The PICSI® Dish

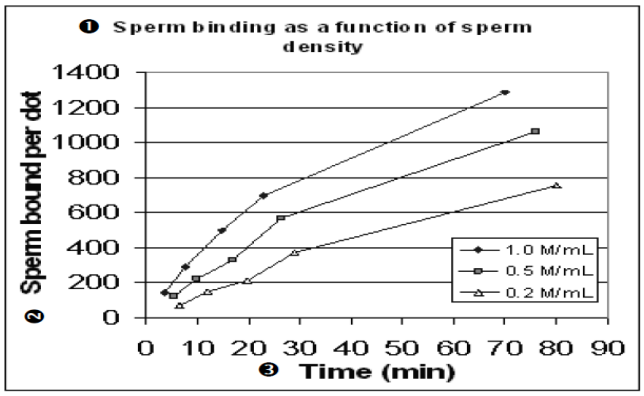


NOTE

Dispose of the device in accordance with local regulations for disposal of medical devices

Figure 2

Sperm Binding versus time an sperm density



1. Sperm binding as a function of sperm density
2. Sperm bound per dot
3. Time (min)

Questions or Comments

Please contact CooperSurgical.

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REFERENCES

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2. *Yagci, A., W. Mark, J. Stronk and G. Huszar. 2010. Spermatozoa bound to solid state hyaluronic acid show chromatin structure with high DNA chain integrity: an acridine orange fluorescence study. J. Androl. 31(6):566-72.*
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Glossary of Symbols

Ref #	Symbol	Title	Description	Standard Development Organization
5.1.6		Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified.	ISO 15223-1
5.1.5		Batch code	Indicates the manufacturer's batch code so that the batch or lot can be identified.	ISO 15223-1
5.4.3		Consult instructions for use	Indicates the need for the user to consult the instructions for use.	ISO 15223-1
5.3.4		Keep dry	Indicates a medical device that needs to be protected from moisture.	ISO 15223-1
5.2.4		Sterilized using irradiation	Indicates a medical device that has been sterilized using irradiation.	ISO 15223-1
5.4.2		Do not re-use	Indicates a medical device that is intended for one use, or use on a single patient during a single procedure.	ISO 15223-1
5.2.8		Do not use if package is damaged	Indicates a medical device that should not be used if the package has been broken or damaged.	ISO 15223-1
5.3.6		Upper limit of temperature	Indicates the upper limit of temperature to which the medical device can be safely exposed.	ISO 15223-1
5.1.4		Use-by Date	Indicates the date after which the medical device is not to be used.	ISO 15223-1
5.1.2		Authorized representative in the European Community.	Indicates the authorized representative in the European Community	ISO 15223-1
5.1.1		Manufacturer	Indicates the medical device manufacturer, as defined in EU Directive 90/385/EEC, 93/42/EEC and 98/79/EC.	ISO 15223-1
n.a.	R_x Only	Prescription device	Caution: Federal law (USA) restricts this device to sale by or on the order of a licensed healthcare practitioner.	21 CFR 801.109
n.a		Product conforms to the Medical Device Directive 93/42/EEC	Signifies European technical conformity.	n.a.

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