INVOcell Insights

America Institute for Reproductive Medicine
Birmingham, Alabama. USA

The Team

Karen R. Hammond, DNP, CRNP
IVF Program Director

Cecil A. Long, MD
Practice Director

Lisa J. Ray, MS, ELD
Embryology Director

Bullet Points

- INVOcell is effective
- High patient satisfaction
- Less time intensive than conventional IVF without compromising pregnancy rates
- Increases access to care for assisted reproduction
- Fewer touch points with this streamlined process

Practice Overview

America Institute of Reproductive Medicine (AIRM) is a small boutique practice established in Birmingham, Alabama in the autumn of 2017 by Dr. Cecil Long. In February 2018, Dr. Karen Hammond joined the practice as the IVF Program Director in February 2018. Embryologist Lisa Ray joined AIRM a few months later.

AIRM performed a total of six cycles of IVF in 2017. After the addition of INVOcell, the number of cycles grew to more than 350 cycles in 2019; with the practice now having

performed nearly 600 INVOcell cases to date. Despite our 3-person essential team and small practice footprint, we estimate AIRM could perform in excess of 600 INVOcell cycles per year, far exceeding what could be performed using traditional IVF with the same clinic resources. As a result, we now predominately utilize INVOcell as the primary treatment option for our "Affordable IVF Program℠", which enables us to achieve our primary goal of providing a high-quality patient outcome at an affordable price.

Unfortunately, the financial burdens of in vitro fertilization (IVF), generally upwards of $10,000 - $15,000 in the United States, restrict access to care for a significant number of patients who would benefit from the treatment. The greatest costs for most IVF cycles are ovarian stimulants and embryology laboratory fees. Current ovarian stimulation protocols stem from a time when fertilization and pregnancy rates were much lower than current times. Since many oocytes are retrieved, many programs have implemented cryopreservation of all embryos with warming and embryo transfer in a subsequent cycle, further increasing the cost of treatment. Improvements in IVF culture media and techniques have also led to better cycle efficiency and higher pregnancy rates. Alternatively, INVOcell has afforded the option of intravaginal culture, eliminating the need for laboratory culture and its inherent costs and risks.

The primary aim of the AIRM Affordable IVF program is to decrease overall cycle costs while maintaining good pregnancy rates and improving access to advanced fertility treatment. To that end, we have implemented a mild ovarian stimulation protocol, oral sedation for the in-office retrieval, intracytoplasmic sperm injection of all metaphase oocytes, intravaginal culture with INVOcell, and fresh embryo transfer.

Our "Affordable IVF Program℠" (utilizing INVOcell) has been widely accepted and well received across the United States. To date, AIRM has had patients present to the program from 28 states, demonstrating that they still find financial benefits despite traveling hundreds of miles and being away from home for a week. The cost of a cycle is approximately one third the cost of traditional IVF which is significant as the majority of the patients report that IVF would not be financially possible without this program. This affordability also enables patients to potentially undergo more than a single cycle.

Integration of INVOcell into our practice

With the primary goal of decreasing the financial burdens of IVF while maintaining the same high quality care and pregnancy rates, integration of INVOcell into our "Affordable IVF Program℠" program was an easy decision. The embryology costs to the program, inherent liabilities of laboratory culture, and the fees assessed to patient are all greatly reduced.

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We, at AIRM, have also noted that the INVOcell also gives our patients a wonderful bonding experience with her embryo(s). The patient does not have to worry about her embryos mingling with other embryos in the IVF laboratory and at the same time she gets to be a party to the processes that are occurring within her. The positive feedback received from patients is amazing. Patients frequently report that they "feel pregnant" while the INVOcell is in place and relish the opportunity to nurture their embryos while in culture.

Clinically, the laboratory workload is decreased with INVOcell. No fertilization checks, no daily observation of the embryos, no worries with taking the embryos in/out of the incubator, essentially no risk for laboratory error. For these reasons, we are able to perform substantially more overall cycles with the use of INVOcell. In addition, perhaps there is an advantage for the developing embryos to adapt to maternal movement and temperature fluctuations. The reduced patient interaction and clinic workload (and staffing requirements) further highlight the advantages of INVOcell during the Covid pandemic as there are much fewer touch points with this streamlined process.

We originally planned to offer INVOcell only to patients for whom finances were a concern. However, after seeing the simplicity, acceptability, embryo quality, and pregnancy rates, all patients are now offered INVOcell. It has simplified the entire process with no loss of quality or pregnancy rate within certain age groups. There is no situation for which INVOcell is not recommended.

Embryology Prospective

The INVOcell in the laboratory setting offers some unique protocols to be used. We are an all ICSI (Intracytoplasmic Sperm Injection) center. Once the oocytes are retrieved, the granulosa cells are partially stripped immediately to assess oocyte maturity. All metaphase 1 and 2 oocytes are then immediately injected. Patients have an opportunity to watch the entire procedure from the retrieval room via a monitor connected to a camera on the micromanipulation microscope. The patient and her partner or support person can see the sperm being immobilized and captured and injection of a sperm into each oocyte. The injected oocytes are then placed into the INVOcell device, and the entire device is passed to the clinician for insertion into the patient's vagina.

When patients return 5 days later, the INVOcell is removed from the patient and the inner vessel is passed to the embryologist. The patient is allowed to see exactly what the embryologist sees. After careful couseling about the number and quality of embryos (as well as the risks, benefits, and alternatives), our clinicians together with the patients decide jointly on the number to transfer, freeze, biopsy or discard. Assisted Zona Hatching (AZH) is performed on each embryo transferred, then the catheter is prepared for transfer.

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Appropriate quality supernumerary embryos can be used in the same way as traditional IVF, including biopsy for PGT-A /PGT-M (genetic screening/sex selection) or cryopreservation for future use.

The process is a definite time saver for our embryologist, since there is no delay in denuding the oocytes or performance of ICSI/Insemination. This process goes from up to six hours to less than 15 minutes. There is no need or ability to check for fertilization. And finally, the process of daily embryo assessment and/or media changes on day two, three, or four is eliminated

Outcomes

Obviously, excellent fertilization rates, and ultimately pregnancy rates, are the primary goals for every IVF program. In our experience, the rates are comparable between traditional IVF and INVOcell. Moreover, the overall patient satisfaction rates seem to be higher with INVOcell. The patient feels she has a more integral role in the overall process. Since the process is streamlined, patients have fewer visits (average of 1.2 monitoring visits), quick retrieval (average 2 minutes), and quick and easy recovery. Even on the day of retrieval, the patient is only in our office for about an hour. Of almost 600 cycles performed, we have had ZERO cases of ovarian hyperstimulation syndrome. Only one patient conceived triplets (trichorionic) despite a two embryo transfer. Even patients who do not conceive report a positive experience with INVOcell. Knowing the pregnancy rate will never be 100%, satisfaction is a very valuable metric**;** and of course, patient satisfaction translates to more referrals.

Unique advantages and perspectives

The joy of providing an opportunity to provide advanced fertility treatments to patients who never fathomed the chance of having the opportunity is immeasurable. Patients also love the chance to have a more intimate IVF procedure by watching the sperm selection and ICSI and actually carrying the injected eggs/embryos instead of worrying about them in the lab.

Having performed so many of these precedures, a number of insights have been discovered along the way. Obviously, patients should be given anticipatory guidance by counseling about each step of the process in advance. More information is better.

We have developed a number of techniques in the laboratory to more effectively deliver the treatment. The INVOcell inner vessel is opened the evening prior to the procedure and placed in an incubator. The morning of the procedure, 0.8 mL of one step media is placed in the inner vessel with the cap remaining open and returned to the

incubator. Just prior to the case, sterile mineral oil is overlayed to allow for maximum control of pH. The inner vessel is once again reincubated and ready to have the injected oocytes placed inside. After the INVOcell is loaded with the injected oocytes, a pipette is backloaded with < 2 µL of culture media, and the injected oocytes are aspirated. The pipette tip is placed inside the media in the laterally positioned inner vessel. The injected oocytes can be observed entering the device and leaving the pipette. Next, the lid is closed tightly on the inner vesseland is tapped on the top with the tip of the pipette for added assurance. The inner vessel is then checked to be appropriately seated in the outer chamber. The lid is then tightly secured and handed off.

The INVOcell and retention device are most easily and comfortably placed in the vagina as a single unit. After the embryologist passes the loaded INVOcell, the clinician places the INVOcell into the the retaining device and folds it over for insertion. The back of the retaining device is positioned behind the cervix and the front is placed behind the pubic bone. After appropriate placement is confirmed the INVOcell is rotated 90º with the index finger so that the INVOcell is horizontal to the vagina. Patients are asked to call if they have any issues with discomfort, but those reports are quite infrequent.

Removing this INVOcell is quite simple. By gentling tugging on the retention device, both the retention device and the INVOcell usually come out at together. Be sure to have a towel handy because vaginal secretions make it slippery. Discard the retention device, open the INVOcell and allow the embryologist to carefully remove the inner vessel without contamination. Occasionally the retention device comes out alone, leaving the INVOcell still in the vagina. The INVOcell can generally be removed by inserting two fingers in the vagina to grasp it for removal. Another technique is to insert a speculum to allow the INVOcell to be grasped between the blades for removal.

To remove the embryos, the embryologist opens the inner vessel, then places it on its side to locate the embryos. The inner vessel is then opened and placed on its side under the microscope. The embryos are usually in one big group and can be retrieved from the inner vessel using a 250ul stripper tip. The embryos are placed in a circle drop of culture media under oil in a 35 mm dish for evaluation. The embryo(s) is/are hatched and prepared for transfer in the usual fashion.

In summary, IVF with INVOcell is a simple, inexpensive, and very rewarding means to increase access to care for assisted reproduction. The small, but real, legal liabilities of laboratory culture are greatly diminished. The entire process is less time intensive compared to conventional IVF without compromising pregnancy rates. High patient satisfaction is a welcome benefit.