



Art and IVF Labs Are Using Smart Materials and Devices for Infertility Treatments

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ABSTRACT

In terms of technology, smart materials are the most important in the twenty-first century. "Smart Materials" have a crucial role in Assisted Reproductive technology (ART). These innovative materials constitute an important part of infertility treatment. Infertility patients are opting for various type of treatments such as intrauterine insemination (IUI), in-vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), Intra morphologically selected sperm injection (IMSI), Physiological Intracytoplasmic Sperm Injection (P-ICSI), Laser Assisted Hatching (LAH), Partial Zona Dissection (PZD), Embryo Biopsy and pre-implantation genetic screening (PGS) or Pre-Implantation Genetic Diagnosis (PGD) and other procedures. IUI and IVF is the most common procedure to treat infertility. The adoption of child is another option for infertile couple. The success rate of IVF is high than IUI. All IUI, OPU or Embryo transfer doing under ultrasound guidance. The design of IVF Lab with smart materials involves highly integrated components and requires interdisciplinary knowledge. Smart materials are capable to reducing the dust and VOCs to prevent the infection and improve culture conditions. For best fertilization we can use either conventional IVF or through direct injection of single sperm into the mature oocyte cytoplasm (ICSI). Hera cell 150i (thermos scientific) CO₂ Incubator and bench top incubator are ideal for embryo culture. Micromanipulator help in fine control to the sperm injection and embryo biopsy by applying positive and negative pressure to the joysticks. This mechanical energy is converted into electrical energy and vice versa by smart materials during their functioning. Therefore, smart materials are predetermined and predesigned to severe as sensors and actuators as required. This paper discusses various types of smart equipment's used in the ART and IVF lab to help in treating the infertile couple and achieving their desire of child.

Keywords: Smart IVF Lab, Incubator, Micromanipulator, Laminar Air Flow (LAF), Microscope, centrifuge Machine, Embryo Transfer, USG Machine, Suction Pump, OPU, IVF/ICSI and PGS/PGD.

I. INTRODUCTION

Smart material and devices for sustainable technologies in the ART and In-Vitro Fertilization (IVF) Lab are very important. The ART and IVF Laboratory should have adequate space to follow good laboratory practice. More specifically: The construction of the laboratory should ensure aseptic and optimal handling of gametes and pre-embryos during all phases of the treatment. The location of storage areas and equipment such as

incubators, centrifuges machine and cryo equipment should be logically planned for efficiency and safety within each working area. Separate office space should be provided for administrative work, such as record keeping and data entry. A general wet area in which washing of equipment, sterilization, etc., is performed, should be separate from the embryo laboratory. Moreover, if fixatives are applied, these analyses should be performed in a separate room in a fume-hood. When commissioning the laboratory, thought should be given to the most recent developments in equipment and facilities. Bench height, adjustable chairs, microscope eye height, efficient use of space and surfaces, sufficient air-condition and the amount of daylight, all contribute to a working environment that minimizes distraction and fatigue. Consideration should also be given to local health and safety requirements.

II. INNOVATIVE PRODUCTS TO COMPLETE THE WHOLE IVF PROCESS

ART and IVF clinics can achieve success by combining the use of tried and tested equipment, scientific insights, knowledge of clinical processes, and an informative training and education programme. We are discussed here smart materials and innovative devices which is use in IVF Labs for giving hope for child to childless couples.

III. THE REQUIREMENT AND BENEFITS OF SMART MATERIALS IN IVF LAB

1. **Smart Structures:** Any ART and IVF Labs need to design smart structure with specified floor. Approximately 100 to 200 square feet area is required for IUI / Andrology Lab. The laboratory equipment used should be adequate for laboratory work and easy to clean and disinfect. Critical items of equipment, including incubators and frozen embryo storage facilities, should be appropriately alarmed and monitored. Gas cylinders should be placed outside or in a separate room with an automatic backup system.
2. **Smart paints:** The walls should also be covered with tiles. Alternately one can cover wall with epoxy paint. 'Ecological' water-based paints are preferred with NO VOC emission. Low-volatile paints with acrylic, vinyl acrylic, or acrylic latex polymers. Epoxy paints emit VOCs (amine) and take several weeks to cure and thus their use should be avoided. Advantage, improved washability and durability. Emission testing on samples is required since amine catalysts can be very persistent. No paint containing formaldehyde, acetaldehyde, isocyanates, reactive amines, phenols and soluble VOCs.

Some examples of smart paints are Benjamin Moore paints, Thomsit, Corian, Lindner, etc., Disadvantage is cost, practical bargain. White coloured, low VOC, low odour epoxy paint with proper burn in period (increased temp and ventilation for a few days initially, with lights on) and assessment for VOCs.

- 2.1. **Floors:** Large vitrified tiles or vinyl sheets or treated marble is preferred. Impervious, sealed, minimum joints. Edges and corners curved for easy cleaning. Slip resistant, non-staining, non-permeable. Solvent free adhesives/vinyl glues – with low VOC emissions. Changing vinyl flooring in neighbourhood caused dramatic fall in pregnancy rate (PR) due to adhesive vinyl glue (Cohen et al, 1997)

3. Smart Modular ART Lab: If anyone wants to be more-strict and is planning to convert the IUI room into an IVF laboratory in future, one can use pressure modules to create positive pressure in the laboratory. however, this is not a must if one is planning just an IUI facility.

3.1. Doors: Sliding door in the IVF Lab areas should be avoided. All doors must be tight-fitting with bottom 'sweeps and perimeter seals (top and edges)' making them 'Air-tight'. Doors preferably glass with coated or steel to reduce the VOCs. In sealed doorpass window preferred to overhand the washed semen sample and follicular fluid to the embryologist for screening. If we have AHU to create the positive pressure easier to maintain if the adjoining operating theatre also has sealed doors and ceiling. Provisions should be made so that doors are wide enough to accommodate large equipment (eg incubators) after the lab becomes permanently sealed and operational.

4. Smart Andrology:

Andrology laboratory also need to design modular with metal to avoid the fixing the dust on wall. Modular lab also helps to reducing the VOCs and easier to cleaning. Andrology lab also need to metal cupboard and racks for keeping the files and other things. Super grade computer also needs to equipped in the andrology lab for maintaining the data digitally and easier to trace. In the andrology lab some equipment's are **essential**: Centrifuge, laminar air flow hood, microscope, Incubator, and test tube warmer. Some equipment's are **desirable**: Phase contrast microscope, Makler chamber, CO2 incubator, Experimental-CASA. Neubauer chamber or the Makler chamber are commonly used. Use of makler chamber is highly recommended as it is very accurate, though more expensive.

In the andrology lab automatic sperm analyzers systems such as CASA are being routinely used in a large volume of work on semenology is being carried out. However, it is not required to run a routine IUI laboratory. Refrigerator is used to store the various chemicals and culture medias to improve their life and quality. The fridge should not be used for any other activity.

Monocular microscope preferably phase contrast to test the semen for count, motility, morphology and other components such as leukocytes /pus cells. The microscope should have 10x, 20x, 40x, and 100x objectives, and a 10x eyepiece.

5. Smart IVF OT:

IVF OT preferably modular with wide metal door is recommended. The sterile area includes operation theatre and embryology lab complex. Operation theatre (OT) must have AC and filter system (HEPA) along with emergency recovery equipment for ovum pick-up.

6. Smart IVF Lab:

Smart IVF Lab should be made with metal as a modular wall and fitted with HEPA and AHU to create the positive pressure to reduce the air contamination. IVF Lab should have facilities for the control of temperature and humidity and must have filtered air and sterility. Mainly they have:

- a. Infrastructure
- b. Equipment
- c. Manpower (Personnel)

6.1. Location of the building: ART and IVF lab must be avoided near petrol pump, chemical godown, factories emitting fine particles, heavy traffic, parking slots, cement godowns, etc. Enquire whether the building or the surrounding site will undergo renovations or demolition in near future. Basic air sampling & determination of VOCs inside and outside the proposed building must be checked.

For IVF lab first floor is ideal due to less disturbance. We recommend to avoid IVF lab setting in the basement because more chance of moisture and fungal infection. Also need to check for any damp area or water seepage before making the IVF lab. Connectivity with lifts/elevators should be there preferably (transportation of gas cylinders, LN₂, etc.). Need to aware in a hospital, should not be near radiation sources like as CT scan, radiotherapy units or near waste disposal areas. It should be away from the exhaust emission areas and the backup power generators. The IVF Lab total area are depending on the expected work load.

Non-sterile and a strictly sterile area: Same space may be used for more than one purpose (no compromise in quality) of service. Sterile and non-sterile cannot be combined. (ICMR ART Regulation bill 2010 & 2021)

6.2. Walls & partitions:

In ART & IVF lab walls & partitions should be non-porous inert material. Cladding with a non-porous material such as panels made from aluminium tri-hydrate are expensive but provide an inert (low VOC), hypoallergenic, easy to clean wall. The ceiling must be composed of a contiguous, solid material, e.g. plasterboard, gypsum panels, Gyprock, Sheetrock®, not tiles, and the need for any access panels must be minimized. Essential access panels must have air-tight, silicone gaskets as sealant. False ceilings should be avoided at all points. May be needed to conceal lights and filters should have solid non porous panels.

6.3. Optional: Closed chambers, benchtop incubators, LASER.

6.4. Experimental: IMSI, embryoscope, polscope.

7. Smart Cryobiology Lab:

This lab is also required modular and ventilated with Laminar Air Flow (LAF) fitted with stereozoom microscope. For gamete storage Liquid Nitrogen cylinder must have and prior use need to fill LN₂ and check any leakage to avoid and loss. Nitrogen tanks should be cleaned and sanitized at least every year.

8. Superb AHU:

Air Handling Unit (AHU) use to improve air quality. AHU stands alone units (with/without positive pressure), e.g. Austin Air, United States of America (Lab air purifier). Laminar air flow stations, Inline filters for the gas supply to incubators and filters to be kept in incubators.

9. Smart IVF Work Station

IVF-workstation is used because it offers aseptic atmosphere for handling of gametes and embryos. This is prepared to fresh air as per the need of filtration-illumination and meet up the standard, sound & shuddering free. LAF unit is obtainable with vertical-air flow-arrangement. This is IVF work station with stereozoom microscope, display and heat control also. The smart IVF workstation is dual core and semi closed systems for preventing fluctuation of temperature, air quality and contamination. The major purpose of laminar-flow-cabinets is to filter atmospheric air twice, through HEPA filters with a corrected performance rating of 99.99% with cold-dispersed oil particles (DOP) and 99.97% with hot-dispersed oil particles (HDOP), thus retaining all airborne particles of 0.3-micron or larger. The filters are designed to remove every particle that

hits the HEPA filter. With the help of a technically-balanced blower, you will be able to receive great airflow all around the HEPA filter and on the IVF workstation. The blower is consisting of a ¼ H.P. motor and operates at lowest sound possible (Shivani Scientific, (2020).

10. Smart Incubator

A minimum number of two incubators is recommended. Incubators should be frequently cleaned and sterilized periodically.

11. Smart UPS as a power backup:

All ART and IVF laboratories should have an automatic emergency generator backup in the event of power failure.

12. RI witness:

Correct handling and identification of patients and their gametes and embryos Written procedures should be present describing the various phases of IVF techniques. Rules concerning the correct handling and identification of gametes and embryo samples should be established by a system of checks and, where needed, double-checks. Proper training of all the laboratory staff according to these procedures is mandatory. • All material obtained from the patients, i.e. tubes with blood, follicular fluid and spermatozoa, should bear unique identification of the treated couple. • Incubators should be organized in order to facilitate identification of embryos, oocytes and spermatozoa. • Verification of patients' identity should be performed at critical steps: before ovum retrieval, at semen recovery and embryo transfer procedures. • Double checks need to be considered at least at: insemination of oocytes, replacement of embryos, embryo freezing and thawing. Written validation of all critical steps in each patient's file is essential.

13. Smart Micromanipulators:

This is an inverted microscope which is used to sperm crushing, sperm selection, oocyte holding, micro injection under a microscopic vision, where a level of accuracy of progress is needed that can't be achieved by the without help of human hand. It may normally consist of an input of joystick, a machine for controlling the choice of movement during work and a production division with the resources of asset a holding needle and injection needle to hold for injection or manipulation the gametes as required.

14. Stereo-zoom Microscope:

The stereo zoom microscope is an optical microscope is planned for small magnification observation of object, searching of oocyte form aspirate of follicular fluid during OPU, usually using beam of light reflected from object surface rather than transmitted through it. The stereo-microscope is frequently used to study the surfaces of live sample or to carry-out close-work like as dissection of seminiferous tubule (in case of TESA), micro-surgery, watch assembly, circuit panel production and crack surfaces as in fracto-graphy and [forensic engineering](#).

15. Suction Pump:

Initially oocyte or follicular fluid aspiration was performed by manually using a syringe connected to the needle. This technique was not given suitable and constant pressure which was harmful to the oocyte. Now a day we are using standardized digital suction pump for follicular fluid aspiration in a safest and controlled manner. Suction pump provides a regulated vacuum up to -500 mm Hg for common suction. When press the

pedal then vacuum response is activated on needle tip. We should maintain the suction pressure ideally from 90 – 120 mm Hg and it does depend on clinician personnel experience.

16. Sample Collection Room:

Smart semen collection room need to be equipped with smart LCD andromantic's videos to help in the semen collection to the patients

17. Air Condition (AC):

In any ART and IVF Lab must have AC for maintain the Lab temperature and relative humidity to prevent the bacterial growth / infection. The ideal temperature for an IVF lab is 24 to 27 degrees Celsius, and the ideal relative humidity is 44 to 50%.

18. QC Device:

CO₂ analyser, pH meter, VOC meter and other devices is the key factor for success. IVF Lab results depend upon the strict quality control. Success can be achieved by monitoring air quality, instruments performance, parameter checks. Instruments should also calibrate regularly to achieve success.

We must strict adherence to hygiene at every steps. We follow the protective laboratory clothing & hair nets. We should bear the non-powered gloves and mask during the procedure. Food, gum, drinks and tobacco strictly prohibited in IVF complex. Cosmetic should be minimized and perfumes should be avoided.

19. VOC filter:

Carbon *filters* are specifically designed to remove gaseous elements from the air and may effectively remove *volatile organic compounds and improve embryo quality developments*.

20. Supportive equipment's:

We must include the supportive equipment like as anti-vibration table, table for incubator and other purposes to improve the work quality. Anti-vibration table is very helpful during micro injection and avoid physical damage of oocyte.

21. Laser for embryo biopsy and assisted hatching:

In the beginning of the LAH has allowed the expansion of accurate methods to drill the thicker zone for easy to hatching and enhancing implantation rate. LAH can twist in the history of not an achievement of embryos to implant them in uterine cavity. Three methods are being used; the mechanical technique, that is partial zona dissection with glass microneedles (Cohen et al., 1990), the chemical assisted hatching using acidic Tyrode's (Cohen et al., 1992), and the laser assisted hatching (Strohmer and Feichtinger, 1992)

22. Test Tube Warmer:

Commonly this device is used for maintaining a stable heat of follicular fluid aspirates in round bottom tube. One of the main factors to manipulating of gametes and embryos is the maintaining the optimal temperature. Test tube heating machine is needs verification of its ability to keep fluid at the preferred temperature. Its temperature could differ with fluid quantity and the brand of test tube warming gadget used.

23. Microscope (Basic role of microscope in SA):

Semen-analysis is the first level of screening test during routine-microscopy and leftovers the foundation for the examination of male-infertility. It gives helpful idea concerning the sperm-count ($\times 10^6/\text{ml}$), sperm-motility, viability or higher leukocytes (pyospermia) of in the ejaculate. Phase contrast microscope is

suggested for routine semen analysis. 50-watt light source for this microscope is recommended, preferably binocular (have 2-eyepieces 10X), have a phase-condenser and slot for camera attachment. Microscope should also contain subsequent accessories for semen-examination (Indian fertility Society, 2016):

1. Objective $\times 10$ (with-yellow), $\times 20$ (with-green), $\times 40$ (with-blue) is necessary for evaluation of motility, vitality and counting of sperm and leukocytes.
2. Objective $\times 100$ (white) is oil immersion bright field (for evaluation of sperm-morphology and sperm-vitality)
3. Negative phase-objective $\times 40$ (non-compulsory; for eosin-vitality test)

24. Stripper Handle:

Stripper handle used for oocyte denudation, transferring oocyte one dish to another dish or drop and washing of oocyte or embryos with adding the denuding pipette according to bore size is needed. b. Its volume 0.25 μL to 3.0 μL can be adjusted. c. This handle gives the ideal suction which is ideal for the manipulation of gamete and embryo. d. Denuding pipette handle has available in different models.

25. Centrifuge Machine (SF800):

SF800 is a temperature regulated centrifuge machine which is more suitable for ART laboratory. This machine protects the cold and thermal shock by maintaining ideal temperature, thus designed at improving the recovery of good morphologically selected normal motile sperm pellet and ART results. We can set the program and temperature by manually in SF800. This apparatus has been planned to control and consequently preserve "Critical" inner-chamber-temperature before, during centrifugation and after. This technology for controlling fixed temperature and rotation helps in maintain sperm motility and obtaining good motile sperm pellet (Shivani Scientific, 2020).

26. Role of Micropipettes:

Micropipettes are used in different laboratories like as chemistry lab, biology lab, medicine lab and embryology lab to hold the measure volume. Now micropipettes are commercially available in a various model and capacity. This device facilitates to measure volume in precise manner at every step (Eppendorf, 2020). Some common pipette used in ART laboratories are: 20 to 200 μL , 10 to 100 μL , 100 to 1000 μL , 2 to 20 μL . In these pipettes we use sterile individual packed pipette tips 200 μL and 1000 μL for transferring the media and making the micro drops for micro culture or washing the oocyte or embryos in aseptic manner. We recommend sterilization with ETO or autoclave (if pipettes are autoclavable) before use.

27. Computer and Printer:

Now a days mostly all departments need smart computer for record keeping digitally as a soft copy. Printer also need for printing the report and other documents. Computer use for all the purposes like as email, data entry and storage etc.

28. Construction Materials:

It must be careful about the material using for making IVF Lab. Should follow the ICMR guideline or ESHRE or ASRM or any other good laboratory practice guideline for designing the smart ART Lab.

29. Non-Construction Materials:

All plastics and glass wares are the non-construction materials choose sterile and nontoxic for the gamete and embryos. Glassware and disposable items used for preparation of culture media should be of tissue culture grade and dedicated for this purpose alone. Culture media, or reagents used in their preparation, should be of a purity appropriate for the purpose.

IV. CONCLUSION

Since the procedure began a few years ago, there have been several new techniques introduced, aimed at expanding ART indications: freezing of oocytes and ovarian tissue, in-vitro maturation of oocytes, intracytoplasmic sperm injection, TESA sperm injection, embryo biopsy and physiological ICSI (P-ICSI). Lasers can also be used to improve implantation, especially in frozen thawed embryos, by drilling the zone. To ensure the IVF lab setting place, floor, paints and over all materials are non-toxic to gametes and embryos, we should be aware of this. All culture medias and plastic were should be purchase from authorized vendors with care of IVF Grade material. However, additional studies are needed before establishing an ART and IVF clinic and registration is required from ICMR for the clinic to run properly.

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