Sahoo et al. Scr Med. 2025 Mar-Apr;56(2):353-67. DOI:10.5937/scriptamed56-53412

CURRENT TOPIC

Electrospun Nanofiber Meshes: Advancing the Science of Hernia Repair

Chandan Kumar Sahoo,[1] Vishal Kumar Parida,[1] Hitesh Chopra,[2] Inderbir Singh[1]

Abstract

Hernia repair continues to be a major barrier in surgical practice, thereby necessitating the continued research for the development of novel methods for hernia repair which mainly focuses on patient compliance. This review paper focuses on the developing paradigm of the nanofiber meshes for the treatment of hernia. This review article summarises the conventional methods for hernia repair, development of the nanofiber mesh, their properties, characterisation and biological evaluation. The review outlines the advantages and disadvantages of nanofiber mesh being used for hernia repair. This review also highlights recent research work carried out on nanofiber mesh for hernia repair and different patent and marketed nanofiber mesh developed for treating hernia. In the end, this review promotes the use of nanofiber meshes as a viable direction for developing the area of hernia repair, providing better patient outcomes and addressing the shortcomings of conventional approaches.

Key words: Nanofibers; Surgical mesh; Herniorrhaphy; Polypropylenes (PP); Polycaprolactone (PCL).

1. Chitkara College of Pharmacy, Chitkara University, Punjab, India.
2. Department of Biosciences, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India.

Citation:
Sahoo CK, Parida VK, Chopra H, Singh I. Electrospun nanofiber meshes: advancing the science of hernia repair. Scr Med. 2025 Mar-Apr;56(2):353-67.

Corresponding author:
INDERBIR SINGH
E: inderbir.singh@chitkara.edu.in
HITESH CHOPRA
E: chopraontheride@gmail.com

Received: 13 September 2024
Revision received: 9 November 2024
Accepted: 9 November 2024

Introduction

Hernia is any projection or bulging of an organ through the cavity wall where it is originally located.[1] Hernias can be uncomfortable and occasionally come with excruciating pain that gets worse when you urinate, lift heavy objects, or strain. When the protruded tissue grows and eventually gets caged then the hernia becomes strangulated. Strangulation will stop the flow of blood, which can cause an infection, necrosis and other potentially fatal problems.

The most frequent or common hernia in both men and women, inguinal hernias occur in about 25 % of men and 2 % of women.[2] Since there is a lack of data from under-developed nations, the precise prevalence and occurrence are unknown. Hernias are thought to be distributed anatomically and by gender similarly to most of the developing as well as developed nations. Adults typically experience the majority of their hernias in the groin region. Two thirds of the groin hernias are indirect and one third of them are direct, accounting for around 75 % of all hernias. The most frequent hernias in both male and female are indirect inguinal hernias, which tend to occur more frequently on the right side. Ten percent of all hernias are incisional and ventral. Femoral hernias make up just 3 % of all hernias. Children can develop strangulated hernias 15 %–20 % of the time, with infants under 6 months of age accounting for almost 50 % of these cases.

Classification of hernia

Hernias are classified into different types like inguinal hernia (75 % of all hernias are of the inguinal variety, which is the most frequent type); femoral hernia (a common type of hernia in the groin, adipose tissue may bulge[3]); hiatal hernia (a common type of hernia that can develop throughout the course of a person's life; the upper part of the stomach ascends through the opening in the diaphragm[4]); incisional hernia (bulging of the tissue through a previously weakened abdominal wall incision[5]); umbilical hernia (type of ventral hernia located at or near the umbilicus[6]); perineal hernia (when pelvic floor muscles are not strong enough, an organ or piece of tissue might press into the abdominal cavity and cause a perineal hernia[7]) and ventral hernia (any hernia that develops in the vertical midline of the abdomen is referred to as a ventral hernia). Umbilical hernias and many incisional hernias are ventral hernias. A ventral hernia above the belly button is referred to as an "epigastric hernia".[8] Another type of hernia that occasionally occur through the *linea alba* below the umbilicus in contrast to epigastric hernias are referred to as "hypogastric hernias".[9]

Conventional methods of treating hernia

The typical course of action for a symptomless hernia is to monitor and wait, however this might be harmful for some forms of hernia like femoral hernias. Forty percent of femoral hernias cause bowel strangulation within two years of the diagnosis. It is yet unknown if non-emergency surgery is beneficial for inguinal hernias repair.[10] Most physicians and health regulatory bodies often do not consider for surgery at first and they go for wait and watch approach but if the hernia is severe then they consider for surgery. Here are some treatment approaches.

Open hernia repair surgery

A groin cut or incision is done during an open hernia repair. It is established which hernia "sac" the intestine protrudes from. The surgeon next pulls the hernia back into the abdomen and applies stitches or synthetic mesh to reinforce the abdominal wall. After surgery, the majority of patients are able to go home within a few hours and they normally recover quickly. After surgery, one should avoid strenuous activity for a month.[11] Some non-mesh open hernia repair techniques such as Shouldice's repair and Schley's repair needs to be explained here. Shouldice repair is a surgical method developed in the early twentieth century by Dr Edward Earle Shouldice for correcting inguinal hernias.[12] Schley's inguinal hernia repair is entirely a tissue repair procedure that was first published in the early twentieth century as an improvement on Bassini's repair. The external obliquely aponeurosis is used to fortify the inguinal canal's weak posterior wall and decrease the enlarged deep inguinal ring.[13]

Laparoscopic hernia repair surgery

A laparoscope, a narrow telescope-like device, is inserted through a very small incision at the umbilicus during laparoscopic hernia repair. The patient undergoing this surgery has to go through a health examination before the surgery, which involves an electrocardiogram (ECG), a history, a physical examination and potentially lab testing, because general anaesthetic is often utilised for this treatment.[14] The patient won't feel any pain during this operation. A laparoscope, which is attached to a tiny video camera no longer than a dime, provides an "inside view" of one's body that is displayed on television displays in the operating room. The abdomen is expanded using a harmless gas (carbon dioxide) for the doctors to see the internal organs and to operate. The peritoneum, which lines the inside of the abdomen, is cut to demonstrate the fragility of the wall of the abdomen.[15] Mesh is placed from the inside to plug the gaps in the abdominal wall and strengthen the tissue. After the procedure is complete, the small abdominal wounds are stitched or covered with medical tape.[16] After a couple of months, the incisions are hardly noticeable. Laparoscopic hernia surgery has benefits such as a quicker return to work (days as compared to weeks), three little scars as opposed to a single bigger incision and a shorter recovery period.[17]

Robotic hernia repair surgery

Similar to laparoscopic surgery, robotic hernia repair involves making small incisions, using a tiny camera, inflating the abdomen and projecting the interior of the abdomen onto television screens.[18] In contrast to laparoscopic surgery, robotic surgery allows the surgeon to operate the surgical equipment while seated in the operating room and using a console. Currently, robotic surgery is

used to treat some smaller hernias or weak spots as well as to repair the abdominal wall.[19]

Watchful waiting

For small, asymptomatic hernias, a watchful waiting approach may be recommended. This involves monitoring the hernia with regular check-ups and avoiding activities that may aggravate the hernia, such as heavy lifting. If the hernia grows or causes symptoms, surgery can be recommended.[20]

Surgical mesh application

In hernia repair procedures, surgical mesh is a medical device frequently utilised to strengthen weakening or damaged tissue, supplying additional support and lowering the chance of hernia recurrence. Basically, there are two types surgical mesh, one is artificial/synthetic mesh which is most frequently used, made up of materials like polyester or polypropylene (PP)[21] and the other one is biological mesh which is derived from human or animal tissues, often used in special cases where synthetic mesh may not be suitable.[22]

Surgical mesh is employed as reinforcement for any weaker or damaged tissue near the hernia site; by adding to the strength, mesh lessens the chance the hernia may recur.[23] Mesh placement can be done by three different ways: onlay (overlay) - a covering that is stitched over the top of the vulnerable spot; sublay - it is positioned underneath the muscle or connective tissue and commonly used during open procedures[24] and inlay (underlay): Laparoscopic or minimally invasive procedures frequently use an inlay placed into the muscle layers.[25]

Mesh can be fixed at the hernia site by sutures where mesh is fixed in place with either absorbable or non-absorbable sutures or it can be fixed by staples or tacks where mesh is fastened using these staples or these meshes are fixed with the help of glue during surgeries.[26]

Commercially available (Table 1) surgical mesh products provide surgeons and patients with cutting-edge options for hernia repair. These meshes, which are typically made from biocompatible polymers like polyethylene or polylactic acid are intended to provide a strong yet lightweight scaffold, promoting tissue regeneration and minimising inflammation.

In ongoing studies new methods and materials are always being investigated in research for mesh development, which impacts on patient outcomes in which new technologies work to enhance patient outcomes while reducing issues that can arise.

Table 1: Marketed nanofiber mesh for hernia repair

N	Product	Company	Mesh properties
1	Dextile™ Anatomical Mesh	*Medtronic*	3D shaped mesh made from non-absorbable single filament polypropylene (PP) textile.
2	Parietene™ DS Composite Mesh	*Covidien*	2D shaped mesh containing absorbable synthetic polymer film and PCL (polycaprolactone) as a binder.
3	Herniamesh®	*Herniamesh® SRL*	Individual-filament PP with various shapes and sizes.
4	Phasix™ Mesh	*Becton Dickinson*	Poly-4-hydroxybutyrate (P4HB), biologically generated, totally resorbable substance, is used to make a knitted monofilament mesh scaffold.
5	Proflex®Mesh	*Samyang Biopharmaceuticals*	Synthetic, lightweight mesh with partial absorption (PP amount 30 g/m^2)
6	Duatene™	*Sofradim Production*	3-D device pore size: Onlay: 1.6 × 3.1 mm. Underlay: 1.3 × 1.8 mm/1.1 × 2.0 mm. Weight: Onlay: 54 g/m^2. Underlay: 97 g/m^2
7	OviTex	*TELA Bio*	Its biological material derived from ovine rumen. Contains permanent PP polymer or resorbable polyglycolic acid (PGA) polymer.
8	Optilene	*B. Braun*	Monofilament mesh containing non absorbable PP and polyethylene. Size varies from 0.2 m to 5 m.
9	Versatex™ Monofilament Mesh	*Covidine*	Mesh size: 5 × 7 cm to 25 × 30 cm Fabric weight (g/m^2): 24 g/m^2 to 100 g/m^2.

Gruber-Blum et al[27] used *Adhesix* and *ProGrip* meshes for hernia repair. *Adhesix* is a self-adherent, double-sided mesh available from *AH*, *Cousin Biotech* and *Bard Davol*, comprising of two components. *Adhesix* is a knitted, single filament PP mesh with a smooth side and a rough side, both covered in a resorbable layer of polyethylene glycol (PEG) and polyvinylpyrrolidone (PVP). PEG and PVP combine to create a hydrogel in the presence of moisture that takes five minutes to crosslink to the underlying tissue. Mesh is approximately 40 g/m^2 following PEG/PVP absorption.[27]

A self-gripping multi-component mesh called *Parietene ProGrip* available from *Sofradim* production is comprised of a fixed single fill PP mesh that is coated by a layer of micro grips made of resorbable polylactic acid (PLA). The PP mesh features pores of 1.5 × 1.0 mm and has an approximate weight of 40 g/m^2. The inclusion of the degradable component results in an augmentation of the mesh's weight to around 80 g/m^2.

Preparation of nanofiber mesh

The process of fabricating a nanofiber mesh for hernia repair entails constructing a nanofibrous framework that can be utilised to strengthen and mend compromised tissues during hernia surgery. This mesh serves to offer structural reinforcement, alleviate tension on the mended tissue and mitigate the likelihood of hernia reoccurrence. The electrospinning technology is frequently used to fabricate nanofiber mesh for hernia repair applications.

The choice of polymers for the preparation of nanofiber mesh for hernia repair is a crucial aspect that influences the performance, biocompatibility and overall success of the surgical intervention. Various polymers are employed in the fabrication of nanofiber meshes and some commonly used polymers are PP which is a thermoplastic polymer and widely used in hernia repair meshes due to its durability and ability to resist degradation over time.[28] PLA and PGA are other biodegradable polymers that are often used in combination to create a composite mesh. They gradually degrade over time, allowing for tissue integration and regeneration.[29] PLA and PGA are considered biocompatible and its use in hernia repair meshes can reduce long-term foreign body responses compared to non-biodegradable alternatives.

Electrospinning

Electrospinning is a widely utilised and adaptable technique for producing nanofiber meshes, which find applications in several fields, including as the fabrication of hernia nanofiber mesh. An electric field is employed to transform a polymer solution or melt into a seamless fibre.[30] The resultant nanofibers are an appealing material for use in biomedical applications because of their high surface area-to-volume ratio and simplicity of customisation.

To make a hernia nanofiber mesh, the polymer is dissolved in a suitable solvent to form a polymer solution or melt, which is subsequently utilised for electrospinning. Subsequently, a syringe connected to a high voltage power supply and containing the polymer solution is utilised.[31] An elevated voltage is applied to the syringe while a conductive collector is placed at a distance from the tip of the syringe. The polymer solution is expelled from the syringe tip and transforms into a slender stream due to the influence of electrostatic forces. The refined jet is further elongated and solidified to generate a constant nanofibrous mesh on the collector.[32]

The features of the nanofiber mesh can be modified by modifying several electrospinning parameters, such as voltage, flow rate, separation distance between the syringe tip and collector and the composition of the polymer solution (Figure 1). In order to produce a hernia nanofiber mesh that possesses the required mechanical strength, porosity and biocompatibility, it is possible to enhance these specific attributes through optimisation.[33]

Electrospun hernia nanofiber meshes offer several advantages compared to traditional mesh materials, such as reduced inflammation, improved tissue integration and a decreased risk of adhesion formation. Moreover, the nanofibers' elevated surface area to volume ratio promotes cellular adhesion and growth, hence expediting the healing process.[34] Electrospinning is a highly efficient technique for producing nanofiber meshes for hernia repair. This method has the potential to improve patient outcomes and reduce the complications associated with traditional mesh materials.

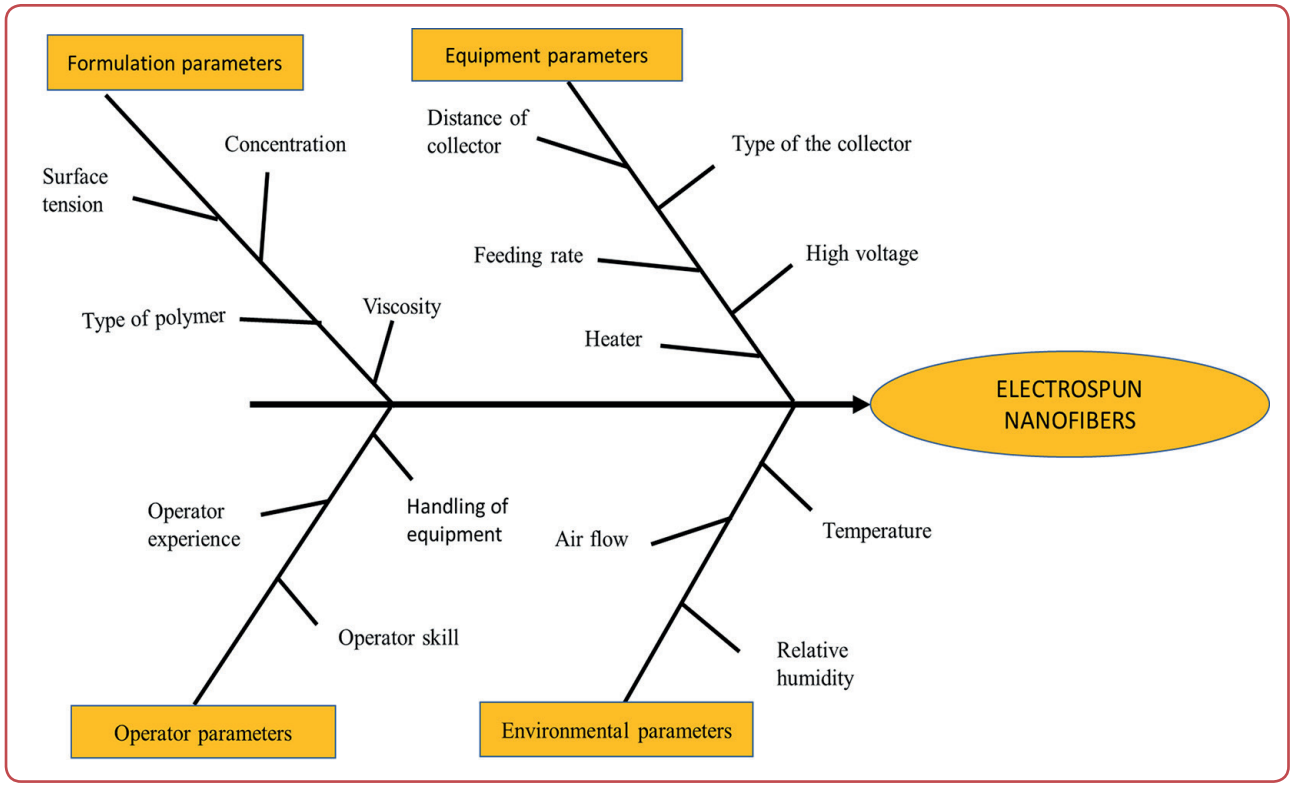

Figure 1: Different parameters affecting electrospun nanofibers

Properties of the nanofiber mesh

The mechanical properties of nanofiber mesh have a significant impact on its suitability for various applications, including wound healing and hernia repair (Figure 2).[35] These qualities have an impact on the mesh's capacity to withstand structural loads, endure physiological stresses and seamlessly merge with adjacent tissues. The following are the mechanical characteristics that are often considered while evaluating nanofiber meshes:

- Elasticity and tensile strength. Poor functional outcomes or a hernia recurrence could occur from the mesh becoming stressed or losing tensile strength. In order to endure the forces generated on the abdominal wall, materials used in surgical meshes must have the minimum mechanical qualities required. A healthy adult's maximum intra-abdominal pressure is thought to be around 170 mm Hg and is produced when they cough or leap. The mesh matrix's resistance to external stresses is improved by the incorporation of nanofibers, giving the weaker or injured tissue in hernia repair better support. This increased tensile strength is especially useful for regions like the abdominal wall hernias that are more susceptible to mechanical stress.[36]

- Porosity. The response of the tissue to the prosthesis is greatly influenced by porosity. Porosity and pore size plays a major role in bacterial growth and cell division. The main places where bacterial colonies are established are between pores and fibres.[37]

- Surface area to volume ratio. Nanofiber meshes have a very high surface area to volume ratio, which makes them ideal for applications that require high surface area, such as tissue engineering and drug delivery.[38]

- Weight. Depending on their weight, prosthesis can be categorised as heavy weight (HW), medium weight, between 50 and 80 g/m^2, light weight, between 35 and 50 g/m^2. Or ultra-light weight, less than 35 g/m^2. The presence of less material in light weight meshes indicates that a less severe foreign body reaction can be expected. Enhanced tissue integration is accomplished by a less inflammatory reaction.[1]

- Tunable biodegradability. The control over

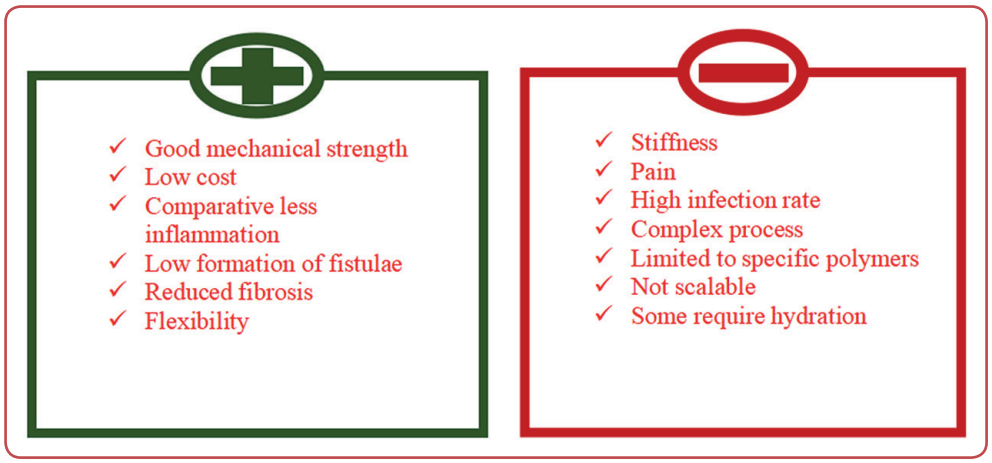

Figure 2: Advantages and disadvantages of nanofiber mesh for hernia repair

the biodegradability of nanofiber meshes can be achieved through the careful selection of polymer material, as well as the adjustment of fibre diameter and pore size. This characteristic renders them highly ideal for a range of biomedical applications, including hernia repair.[39]

- Enhanced cell adhesion and proliferation. Nanofiber meshes possess a large surface area and porosity, which creates an optimal setting for cell attachment, proliferation and differentiation. Consequently, they are highly valuable in the fields of tissue engineering and regenerative medicine.[40]

- Tailored surface chemistry. Nanofiber meshes can be readily altered at the molecular level to attain precise functionalities, such as bioactivity, anti-bacterial qualities, or drug release capabilities. This renders them highly valuable for a diverse array of biomedical applications.[41]

- Biocompatibility. Many of the materials used to produce nanofiber meshes, such as collagen, gelatine and poly (lactic-co-glycolic acid), are naturally derived and biocompatible, making them suitable for biomedical applications.[42]

- Material absorption. Surgical meshes can be constructed from materials that are either absorbable or not. Non-absorbable meshes provide long-term stability, can sustain mechanical demands and are simple to shape intraoperatively. However, there have been reported side effects including mesh erosion, adhesions and mesh stiffness over time.

Characterisation of nanofiber mesh

Structural morphology

The morphology of nanofiber mesh refers to the physical structure and arrangement of the nanofibers within the mesh. The morphology of the mesh can be controlled by various factors during the electrospinning process, such as the polymer concentration, solvent type, electrospinning parameters and collector design.[43] Some of the key morphological features of nanofiber mesh include:

- Fibre diameter: The fibre diameter is a crucial morphological characteristic of nanofiber mesh and it can be regulated by manipulating the electrospinning settings. The fibre diameter typically spans from a few nanometres to several hundred nanometres.

- Pore size: The nanofiber mesh's pore size is dictated by the organisation and density of the nanofibers and it may be regulated by modifying the collector design and the electrospinning parameters.[44]

- Porosity: The porosity of the nanofiber mesh is dictated by the diameter of the fibres, the density at which they are packed and their alignment. Increased porosity results in a larger surface area that can be utilised for cell adhesion and proliferation.[45]

- Surface roughness: The nanofiber mesh's surface roughness is determined by the fibre diameter, the electrospinning process and the collector design. An uneven surface might enhance the attachment and growth of cells.[46]

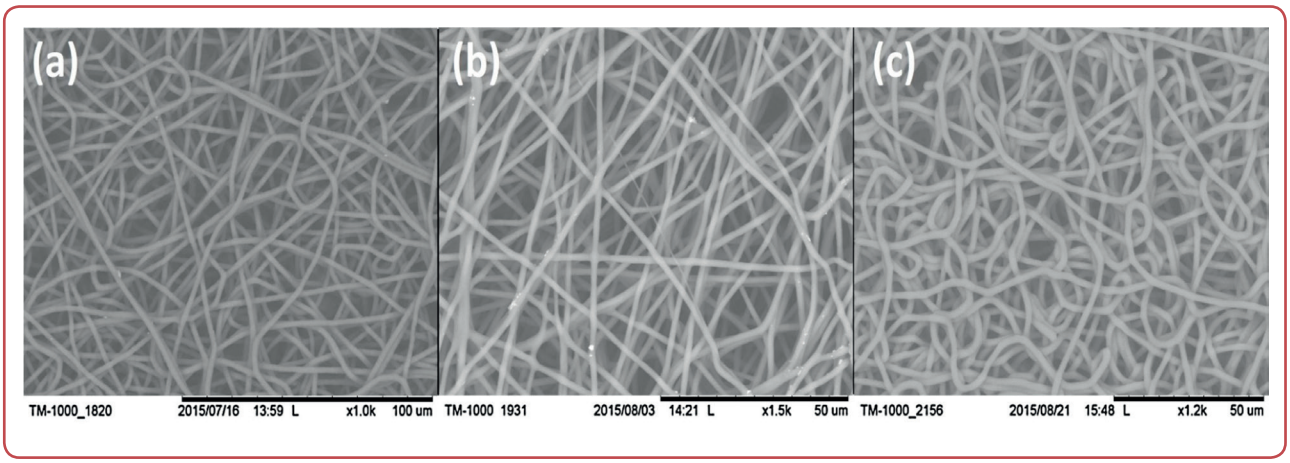

Figure 3: Scanning electron microscopy (SEM) images of different electrospun nanofibers[31]

Morphological analysis

Scanning electron microscopy (SEM): SEM is a commonly employed analytical tool for visualising the structure and shape of nanofiber meshes. The system offers high-resolution imaging of the nanofibers, allowing for precise measurements of their diameter, alignment and pore size.[47]

Figure 3 displays scanning electron microscopy pictures of different poly-capro-lactone (PCL) scaffolds, with and without drugs synthesised by Ivan et al.[31] The analysis uncovered that the primary disparities seen among the three different scaffolds are associated with the diameters of the fibres. To be more exact, the inclusion of irgasan (IRG) resulted in a decrease in the mean diameter of the fibres. The identified fibres demonstrate a remarkably uniform size compared to previous investigations of PCL fibres.

Fourier transform infrared spectroscopy (FTIR): FTIR spectroscopy is employed to analyse the chemical composition of a nanofiber mesh. Spectroscopy can yield data regarding the functional groups inside the polymer and can be utilised to verify the existence of particular biomolecules. ATR-FTIR spectroscopy was conducted on PCL, gel and PCL gel samples using a spectrum 100 apparatus (Perkin Elmer) equipped with a diamond crystal. Spectra were obtained at room temperature within the wave number range of 4000–600 cm^{-1}. The data was collected by performing an average of 32 scans at a resolution of 4 cm^{-1}. The analysis of spectra was conducted using spectrum software.[48]

X-ray diffraction (XRD): XRD is used to determine the crystal structure of the nanofiber mesh. It can provide information on the degree of crystallinity of the polymer and its orientation within the mesh. X-ray diffractometer (*Inel*, Equinox 3000) patterns of pure ofloxacin, CECS/PVA, PCL, ofloxacin/CECS/PVA and ofloxacin/PCL were all recorded. By taking into account de-convoluted XRD peaks, the level of the nanofibers' crystallinity was determined by the equation,[49]

$$x_C = \frac{A_C}{A_C + Am} \times 100$$

Differential scanning calorimetry (DSC): DSC is used to analyse the thermal behaviour of nanofiber mesh. It can provide information about the glass transition temperature, melting temperature and crystallisation temperature of the polymer.[50]

Water contact angle: The water contact angle of the nanofiber mesh can be used to determine its surface energy and hydrophilicity. A low contact angle indicates a more hydrophilic surface, which can be beneficial for promoting cell adhesion and proliferation. Gel membranes had a water contact angle of 80.4 ° ± 2.8 ° while PCL membranes showed a strong hydrophobic behaviour of 138.9 ° ± 1.1 °. PCL-gel nanofibers were less hydrophobic than PCL ones (99.9 ° ± 21.6 °) because they contained amino and carboxyl functional group.[48]

Biological evaluation of nanofiber mesh

The biological assessment of nanofiber mesh for hernia repair involves thorough examination to

verify its safety and efficacy. This assessment comprises both *in vitro* and *in vivo* research aimed at investigating cell compatibility, tissue integration and inflammatory response. The mesh's biocompatibility, degradation rates and mechanical qualities are carefully examined to ensure its suitability for implantation. Thorough biological assessments confirm the nanofiber mesh as a feasible choice for hernia repair, therefore enabling safer and more effective surgical procedures.

(1) Biocompatibility test

In a study conducted by East et al[51] scaffolds made of PP mesh modified with PCL nanofibers were subjected to MTS test (cell proliferation assay test) to determine their biocompatibility. The groups that were put to the test included PP mesh, PP/PCL and PCL nanofibers. The MTS test was carried out to evaluate cell metabolic activity on days 1, 3, 7 and 14. Increased metabolic activity was observed throughout the study, the collected data showed that all of the examined samples (PP, PP/PCL and PCL) are biocompatible.

Another study conducted by Afewerki et al[39] in which they evaluated the biocompatibility of the engineered PCLMA:GelMA, PCL and GelMA nanofiber through subcutaneous implants on the dorsal region of rats for 5 days. The investigation firstly confirmed that all of the groups examined had normal-appearing surrounding tissue and no necrosis. Comparing the crosslinked PCLMA:GelMA (70:30) implant to the PCL and GelMA samples, a considerably higher level of tissue response of the capsule around the PCLMA: GelMA implants was seen. When compared to PCL and GelMA, the PCLMA:GelMA (70:30) showed a significantly higher number of blood vessels.

(2) Cell culture studies

In a study conducted by Kaya et al[40] wherein they developed a dual mesh consisting of PGS/PCL nanofiber layer (poly-glycerolsebacate/polycaprolactone) and PU (polycarbonateurethane) layer for abdominal wall hernia repair.

By cultivating human umbilical vein endothelial cells (HUVECs) on two sides of the dual meshes for a period of 14 days, they evaluated the mesh's capacity to support tissue growth in the abdominal wall and prevent the visceral adhesion at the other side. The cells that were grown on the PGS/PCL layer, which will help with the repair of the abdominal wall, started to spread well as early as the third day and completely covered the surface in just 14 days, but few living cells were discovered on the PU (poly-carbonateurethane) surface. The Alamar Blue cell viability experiment also quantitatively supported the differences in cellular survival on either of the sides.

Using dihydroxyphenylalanine (DOPA) and ofloxacin-loaded carboxyethyl chitosan/polyvinyl alcohol-polycaprolactone (PVA-PCL) nanofibers, Shokrollahi et al[52] created a biomimetic two-sided PP mesh for prospective hernia repair. By inoculating mesenchymal stem cells from adipose tissue (AdMSCs) into the mesh samples for a period of 24 h, they assessed the cell adhesion on the front side of the samples. In hybrid nanofibers, cells containing 0, 5 and 10 wt. % ofloxacin and attached to surface of the samples had a rounded morphology. Additionally, it appears that as the drug concentration increased, there were more rounded cells present. As a result, the cells favoured to cluster and form spherical structures to colonise and spread out across the nanofiber's surface. The results of cell culture study indicated that hybrid nanofibers could stop cell division and growth.

(3) Cytotoxicity study

The cytotoxicity study of the dual mesh consisting of PGS/PCL nanofiber and non-adhesive PU layer was evaluated by Kaya et al.[40] After cell culturing of the mesh for 72 h, they found out that the cells were able to expand across the whole nanofibrous surface, nearly attaining full confluency, while yet retaining their distinctive spindle-shaped morphology. It is obvious from combining the findings of the microscopic analysis and the cellular survival test that the leachable components from the created dual mesh are non-poisonous to cells, having a cytotoxic index of 1.6 and are not toxic to cells.

Mao et al[37] did a comparative analysis of a PP-based composite mesh used to repair hernias in the abdominal wall. The cytocompatibility of PP materials was initially assessed in this study because they may alter cell adherence, growth and cell division on their surface. L-929 fibroblasts were co-cultured with different PP meshes for 5 days. By using the CCK-8 assay, Ying et al were able to determine the prosthetic materials' cell toxicity both before and after the addition of PP meshes and nanofibrous barriers. After a one- and three-day incubation period, all groups develop gradually and multiply healthily.

The different groups' cell viability showed no appreciable variation. The outcomes showed that the PP prosthesis had no cytotoxicity both before and after adding nanofibrous barriers.

Recent advances in development of nanofiber mesh for hernia repair

Enhancing biocompatibility, strength and healing characteristics have been the main emphasis of recent developments in nanofiber mesh for hernia repair. The development of composite materials for increased mechanical strength, the use of electrospinning processes for accurate fibre alignment and the incorporation of bioactive substances like growth factors to speed up tissue regeneration are examples of innovations. Additionally, nanofiber meshes are being customised to meet the demands of individual patients, ushering in a new era of individualised hernia repair options with fewer issues and better results.

Characterisation of nanofiber mesh

East et al[53] created a composite scaffold and tested it in a minipig using regular PP hernia mesh and PCL nanofibers. Testing on the scar tissue's histology and biomechanics followed. They discovered that PCL nanofibers have significant effects on the repair of abdominal fascia with a conventional PP mesh in comparison to the prolene group, they lead to a more uniform distribution of type 1 collagen within the scar, which is associated with a larger density of microvessels and less contractile myofibroblasts. This may mean future shrinkage will be reduced, leading to more clinically beneficial outcomes.

Mao et al[54] created the first composite meshes incorporating nanofibers by combining several PP meshes with the PLGA/PCL NFM (nanofibrous membranes) barrier. In order to ascertain their effectiveness for treating abdominal wall hernias, the researchers conducted trials both *in vivo* as well as in the lab. The PP substrate is crucial for supplying mechanical support and the meshes shown exceptional biocompatibility according to the findings of *in-vitro* tests. The produced C-PP1 (one of the mesh codes assigned by the researchers) mesh demonstrated noticeably better anti-adhesion effects and histocompatibility as compared to bare PP mesh.

By electrospinning an oxidised regenerated cellulose-polycaprolactone combination (ORC-PCL) layer over a PP mesh, UA Sezer et al[55] created a novel composite mesh with anti-adhesive properties. Studies conducted *in vitro* and *in vivo* revealed biocompatibility in ORC-PCL electrospun PP mesh. The *in vivo* studies also showed that ORC-PCL layer on mesh had better tissue compatibility and anti-sticking capabilities than PP-PCL layer. PP/PCL-ORC20 composite mesh composed of approximately 20 % ORC was optimised based on superior mechanical qualities as well as equivalent biocompatibility for curtailing the harmful reactions of ORC acidity, even if a larger concentration of ORC exhibited higher compatibility.

As per a study conducted by Liu et al,[56] six new warp knitted PP meshes were created and their potential for use in hernia repair was assessed. Electrospinning 10 % PCL onto newly created meshes produced two patterned nanofiber mats. Six meshes' mechanical characteristics were on par with those of meshes that are currently on the market and their anisotropy was compared to the characteristics of the human abdominal wall, indicating that they may be useful for hernia repair. The *in vitro* biocompatibility assessment of PP and PP/PCL composite meshes showed that PCL nanoparticles were more conducive to cell attachment and proliferation than bare PP meshes and after 21 days after seeding, cells had virtually completely covered the surface of both materials. Regarding the cellular response on the patterned mats, cells on the loosely aligned nanofibers displayed significantly greater elongation and aligned orientation than those on the random and spiral patterned sections.

Synthetic nanofiber mesh

Kaya et al[40] developed a bifunctional dual nanofiber mesh using solvent casting and electrospinning processes from non-biodegradable thermos-softening plastic polyurethane and biodegradable poly-glycerol sebacate/poly-caprolactone blend. The outcomes showed that the chosen processing method could successfully

achieve the adhesion between two layers. Additionally, this mesh's characteristics were advantageous in terms of elasticity in both dry and wet states. The component of the layer that was electrospun ie, the PGS component, started to disintegrate in the early phases of incubation carried out in outer environment in physiological solution, which was amply confirmed by a significant loss in weight and changes in surface profile and roughness. According to prior *in vitro* cell toxicity screening tests, manufactured dual meshes' degradable components had no hazardous effects on cells from which connective tissue develops. Additionally, the environment friendly electrospun mesh promoted endothelial cell attachment and growth at their surface, in contrast to the nondegradable smooth film, which had the opposite effect.

Giuntoli et al[48] designed a novel composite hernia mesh system which helps in reorganising existing tissues during wound repair, improving mesh amalgamation. The composite hernia mesh system was created using electrospinning where a nanostructured membrane from a blend of PCL and gel is electrospun onto a commercially available hernia mesh consisting of PP. Room-temperature gel, PCL and PCL-gel membranes consisting of nanofibers were created and characterised using morphological, mechanical, thermal and physical-chemical studies. The uniform, ultra-thin PCL-gel nanofibers show good wetting property and suitable hindrance to degradation by enzymes and hydrolysis. Then, human fibroblasts were used to test the multicomponent hernia mesh device's biocompatibility. A rapid and adequate assimilation of the mesh at the implantation site after completion of surgery for repairing abdominal wall hernia was achieved with the help of the nanostructured covering, thereby avoiding any cell toxic effects and promoting cell responsiveness.

Anti-microbial nanofiber mesh

As per a study performed by Han et al,[57] poly(butylene succinate-co-butylene aspartate) (PBSA) was created by adding aspartic acid to a polyester chain made of polybutylene succinate (PBS). Levofloxacin (Lv) was grafted onto a PBSA polymer's surface as an antimicrobial therapy (PBSA-g-Lv). Both P(Asp)-co-PCL and P(Asp)-b-PEG-co-PCL exhibited good mechanical and thermal qualities that made them both appropriate for hernia repair, according to the results. The polyesters also displayed outstanding hydrophilicity, which is critical for encouraging cell adhesion and tissue regeneration. Furthermore, both bacteria's which retains the gram stain and which does not retain the gram stain were resistant to polyesters' antibacterial properties. *S aureus* and *E coli* effectively were killed by electrospun PBSA-g-Lv polyester nanofibers, which also have the ability to stop wound infections. The study by Han et al[57] outlines an effective plan for creating a hernia mesh that is safe and has the desired hydrophilic, anti-bacterial and anti-adhesion qualities.

Fehér et al[58] developed an absorbable poly vinyl alcohol (PVA) mesh. Using an adult human dermal fibroblast cell line, the researchers studied the toxicity of the polyvinyl acid (PVA) solution and nanofibers. On rat and swine models, implantation tests were observed. Diamond and Vandendael scores were employed to gauge adhesion formation. PVA solution and nanofibers have been tested *in vitro* and showed biocompatibility with the cells. The tests carried out at the implantation site on animal models revealed that every sample was assimilated into the surrounding tissue without any signs of a foreign body reaction. The non-absorbable suture line had the average number of adhesions. The designed mesh's biocompatibility was proven. It possesses a non-sticky, toxic free and fine structure that could make it a viable replacement for the hernia mesh portion.

3D printed nanofiber mesh

The purpose of a study conducted by Qamar et al[29] was to investigate the use of 3D printing using fused deposition modelling (FDM) to create customised hernial meshes. Different meshes were constructed with PP and PVA by loading ciprofloxacin HCL and in some meshes ciprofloxacin HCL were not loaded. Each mesh has varied size of pores, shape and thickness of threads in those meshes. PP mesh was printed in a large number in comparison to that of PVA mesh. Researchers examined mechanical properties, drug loading into the meshes and drug release properties of the meshes which were 3D printed. All of the printed meshes had acceptable mechanical characteristics. In contrast to PP-based meshes, the PVA meshes demonstrated a somewhat faster

release. Additionally, *in vivo* tests on rabbit models showed zero indications of non-acceptance of the mesh implant and only mild to moderate level attachment to the adipose tissue. Animals implanted with meshes containing ciprofloxacin HCl showed less body temperature swings and quicker wound healing.

The results of this study proved that FDM 3D printing is a practical and affordable alternative for producing customised meshes with or without medication loading for hernia therapy.

Ballard et al[59] created a PLA mesh by coating gentamicin with the help of 3D printing. Release of gentamicin was tested *in vitro*. It demonstrated antibacterial effects against *S aureus* and *E coli*, with observable zones of inhibition measuring 1.1 and 1.2 cm^2, respectively.

Patented nanofiber meshes for hernia repair

Patented nanofiber meshes for hernia repair are revolutionary medical advancements (Table 2). These meshes have exclusive technology that improves tissue integration, durability and biocompatibility. The goals of these patents are to lessen difficulties and enhance patient outcomes in hernia repair surgery by utilising novel materials for manufacturing techniques. These developments represent a huge step towards creating safer and more successful hernia repair techniques and they offer enormous potential for the medical field.

Commercially available nanofiber mesh for hernia repair

NanoMesh™ LLC, a unit of *Exogenesis* corporation, has announced the successful commencement of the first implantation of its exclusive soft tissue repair device, *Exogenesis nanoMesh*™, in a human subject. Exogenesis hernia mesh is a proprietary hernia repair product constructed using monofilament propylene surface treated with accelerated neutral atom beam (ANAB) technology. ANAB is a low energy nano scale technology used for surface modification and control for various biomedical, optical and semi-conductor applications. On 6 April 2021, exogenesis made a formal submission to the US Food and Drug Administration (FDA) on their *nanoMesh*™ product, completing the second pre-marketing notification application (510(k)). It provides greater biocompatibility than the other surgical meshes available in the market.[69]

The Green Nano Mesh project, financed by the European Union, aims to utilise sustainable resources and green nanotechnologies for targeting hernia operations. A pan-European initiative was initiated to create biodegradable hernia meshes at the nano-and micro-scale using fibrous materials. These products guarantee to improve functional restoration and are manufactured without the use of dangerous procedures and substances. The meshes were fabricated using sustainable raw materials such as poly-epsilon-caprolactone, PLA, pepsin-extracted bovine collage and human recombinant collagen. Scientists created laboratory mesh prototypes by employing various procedures including freeze-drying, electrospinning, supercritical CO_2 technologies, dip coating and green cross-linking methods.[70]

Bacterial nanocellulose is a newly emerging, biocompatible natural polymer that is becoming increasingly used in the healthcare industry. ICMAB-CSIC (Institute of Materials Science of Barcelona) researchers and *B. Braun* surgical, a prominent producer of wound closure medical devices, have partnered to create a surgical mesh using bio-based biomaterial. The initial findings from an animal testing conducted showed encouraging results, which manifest to take innovative steps in designing of nanofibrous meshes for the treatment of hernias.[71]

Some of the potential risks associated with clinical applications of nanofiber mesh for hernia repair include infection risk as there is a risk of bacterial colonisation at the surgical site due to the nanofiber mesh application. Some individuals may experience a heightened immune response to the nanofiber material, leading to a foreign body reaction. Mesh degradation is another risk involved which might lead to hernia recurrence. The long-term durability of the nanofiber meshes for hernia repair is still a subject of ongoing research. The potential for degradation or loss of mechanical strength over time could impact the effectiveness of the repair. Limited clinical data is available regarding the nanofiber mesh for effectively treating the hernia repair.

Table 2: Patented nanofiber mesh for hernia repair

N	Publication number	Title	Country	Year	Objective	References
1	US7235295B2	Polymeric based nanofiber for tissue engineering and drug delivery	US	2007	Development of polymeric nanofiber mainly used for medical prosthesis, hernia repair, wound healing	[60]
2	US20090149875A1	Flat hernia mesh implant	US	2009	Development of flat hernia mesh implant made up of monofilament yarns	[61]
3	US20050228408A1	Flat hernia mesh made up of thread material	US	2005	Flat hernia mesh implant made up of textile thread material	[62]
4	CN204364173U	Hernia mesh containing nano titanium	China	2015	Nano-titanium loaded hernia patch repairs a sticking patch of hernia	[63]
5	US20150196377A1	Hernia repair patch	US	2015	Hernia repair patch inserted into the abdominal wall cavity	[64]
6	US20180071071A1	Hernia repair grafts with anti-adhesion barriers	US	2018	Hernia repair grafts consisting of substrate and a sheet of anti-adhesive material	[65]
7	US9456887	Inflatable hernia patch	US	2016	Inflatable hernia patch used for repairing intra-abdominal hernia	[66]
8	CN105266923A	Light hernia repair patch and knitting method	China	2018	The light hernia repair patch exhibits a concave-convex surface along its longitudinal axis and its pore diameter is more.	[67]
9	CN107756781A	Hernia sticking patch	China	2018	This hernia sticking patch is 3D printed and has adjustable pore sizes and it is characterised by its convenience and efficiency leading to reduction in cost	[68]

Conclusion

Since the release of the first-generation mesh, surgical techniques along with the mechanical and physiochemical properties of surgical mesh have changed. However, the vast majority of meshes on the market are still constructed of PP. Because of their biological inertness and textile mesh structure, these meshes have a tendency to compress over time and trigger a strong immunological response. The main design elements that affect mesh mechanical characteristics and body reaction are filament size, arrangement and porosity. The physicochemical and surface properties of the mesh have been optimised using a variety of methods, but the perfect mesh that fully satisfies all requirements has not yet been discovered. The review also showed that the structure of the prosthetic mesh has received significant attention in order to facilitate placement, fixation and implantation by surgery. Various technologies are being developed to complement laparoscopic procedures as well as enhance the placement and handling of the meshes and facilitate quick, simple and effective surgical implantation of the mesh. New mesh designs are being developed to overcome the drawbacks and difficulties of the first- and second-generation mesh. The development of 3D printed nanofiber mesh for hernia repair is expected to make significant progress. Further research and development may result in even more precise designs that are exactly personalised to each patient's anatomy, reducing problems and speeding up recovery. With the current advancements in the use of 3D printing in pharmaceutical production, tailored, cost-effective and on-demand hernia mesh might operate as a replacement for marketed mesh.

Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

Acknowledgement

Authors are thankful to their parent institutions for the facilities.

Conflicts of interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

Author ORCID numbers

Chandan Kumar Sahoo (CKS):
0009-0009-1348-0895
Vishal Kumar Parida (VKP):
0009-0000-8481-2409
Hitesh Chopra (HC):
0000-0001-8867-7603
Inderbir Singh (IS):
0000-0002-1860-4246

Author contributions

Conceptualisation: CKS, VKP
Writing - original draft: CKS, VKP
Writing - review and editing: HC, IS
Project administration: HC, IS

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