



Research Paper

Fixation free inguinal hernia repair with the 3D dynamic responsive prosthesis ProFlor: Features, procedural steps and long-term results

G. Amato ^{a,*}, G. Romano ^b, T. Goetze ^c, L. Cicero ^d, E. Gulotta ^b, P.G. Calò ^e, A. Agrusa ^b

^a Postgraduate School of General Surgery, University of Cagliari, Italy

^b Department of General Surgery and Emergency, University of Palermo, Italy

^c Institut für Klinisch-Onkologische Forschung Krankenhaus Nordwest Frankfurt/Main, Germany

^d IZSS Palermo, Italy

^e Department of General Surgery, University of Cagliari, Italy

ARTICLE INFO

Article history:

Received 19 July 2019

Received in revised form

26 September 2019

Accepted 25 October 2019

Available online 4 November 2019

Keywords:

Inguinal hernia

Dynamic responsive prosthesis

Biologic response

Tissue regeneration

Tissue scaffolds

ABSTRACT

Background: Static and fixated meshes to repair mobile structures like the groin may seem a procedural incongruence. Inguinal hernia is described as a degenerative disease. Therefore, the objective of disease treatment should be the regeneration of wasted tissue. The fibrotic scar plate, a typical biologic response of conventional static meshes, does not represent tissue regeneration but rather a foreign body reaction. These contrasting aspects seem to be related to high complication rates of inguinal herniorrhaphy. Recent studies concerning the pathophysiology of the groin have led to the development of new concepts for repairing inguinal protrusions. A proprietary designed 3D dynamic responsive implant showing regenerative biologic response is the result of this studies.

Materials and methods: A cohort of 389 individuals underwent open inguinal hernia repair with the 3D dynamic responsive implant following a specific surgical technique. Thanks to the inherent dynamic properties, all procedures were performed without need for fixation of the 3D prosthesis.

Results: The outcomes of the dynamic hernia repair procedure were reduced postoperative pain and minimized overall complication rates, also long term. Moreover, no patient discomfort or chronic pain was reported.

Conclusions: Inguinal hernia repair with the 3D dynamic responsive implant ProFlor seems to represent an effective concept change for the treatment of this widespread degenerative disease. Moving in synchrony with the groin, implanted without need of fixation and acting as a regenerative scaffold, ProFlor™ appears to possess all that is needed for a physiologic and pathogenetical consequent treatment of inguinal protrusions leading to a dramatic lessening of intra- and postoperative complications.

© 2019 The Author(s). Published by Elsevier Ltd on behalf of Surgical Associates Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Inguinal hernia, unlike common perception, is a complex disease occurring in one of the most dynamic parts of the body. Despite frequent occurrence, for some time further study on the etiology of the disease was an almost neglected subject. In the past few decades, pathogenetical investigations have mostly focused on the detection of ultrastructural changes without considering the structural modifications occurring in functional as well as histopathological anatomy [1–3]. Only in recent years have studies regarding these aspects of inguinal disease revealed new evidence

leading to a more defined picture of the pathogenesis, which is typically degenerative [4–8].

Inguinal hernia repair, with an estimate of over 20 million patients yearly, represents one of the most common surgical procedures of all [9]. Several techniques, but no shared treatment concept, characterize the therapy of this disease. Consequently, there is no “Gold Standard”. However, the high number of commercially available, static and passive prosthetic devices would appear to further confirm the trend in this field.

By analyzing the concepts of commonly performed hernia repair techniques and prosthetic devices used for the treatment, it would seem that the physiology of the groin and genesis of the disease are rarely considered [10–13]. Repairing a disease of one of the most motile areas of the body with static or fixated devices may seem a

* Corresponding author. Via Rapisardi 66, I – 90144, Palermo, Italy.

E-mail address: amatomed@gmail.com (G. Amato).

contradiction in terms. Similarly, the biological response of conventional static prostheses that produce a fibrous scar plaque instead of regenerating the degenerated inguinal barrier is inadequate; in a degenerative disease like inguinal hernia regeneration should be the target [14–16].

With this in mind, a concept change in inguinal hernia repair has been considered. One cornerstone in developing a new model of treatment was groin physiology and its motile feature. Another key point, which is the subject of much attention, concerned awareness that the degenerative source of groin hernia could be resolved only through the regeneration of the inguinal barrier dissolved by the protrusion disease. Thus, a new implant has been developed: a 3D dynamic responsive implant for inguinal hernia repair [17]. This 3D multilamellar shaped prosthesis, manufactured in low weight - large porous polypropylene, is intended to be delivered into the hernia opening [18]. It is self-retaining, thanks to its inherent centrifugal expansion which fully obliterates the defect without need for fixation [19]. This 3D prosthesis moves in synchronization with the groin structures, contracting and relaxing with the inguinal musculature. Its steady compliance to inguinal movements allows for an enhanced biological response with the ingrowth of newly formed tissue, which in all aspects corresponds to the typical components of the abdominal wall [20]. The present study is aimed to highlight the features, procedural steps and long-term results of the dynamic inguinal hernia repair technique carried out with this newly conceived 3D dynamic responsive prosthesis.

2. Material and methods

A cohort of 389 patients who underwent inguinal hernia repair with a recently designed 3D dynamic responsive implant forms the body of the report that was designed as a multicentric study. Institutional ethic approval was granted to the investigation. The prosthesis named ProFlor™, manufactured with light-weight, large porous polypropylene and composed of a multilamellar, flower-like structure, having “petals” connected at the center with a small polypropylene ring (produced under license by Inshightra Medical Inc. - USA) was used in all patients (Fig. 1 A). The edges of the petals are made of reinforced polypropylene, to assure springiness, both in the longitudinal as well as vertical axis (Fig. 1B–E).

Two different 3D implant sizes were used:

- 1) one small sized, with a pre-peritoneal disc 60 mm in diameter, (weight 0.77 g, core diameter 25 mm and 15 mm height, with 6 petals);
- 2) one large sized, with a pre-peritoneal disc 70 mm in diameter, (weight 1.51 g, 3D core diameter 40 mm in and 15 mm in height, with 8 petals).

The procedure was performed in 343 men and 46 women. The follow up length ranged from 72 to 12 months. Patient median age was 46.16 years (range 18–84) median BMI 27.43 (range 23–34). The obliterated hernia defects were between 15 and 37 mm. Defects larger than 37 mm, e.g. combined hernias involving all three inguinal fossae, were not considered for enrollment in the study. Local anesthesia was the method of choice in all primary hernia repair. Only in the 42 patients with recurrent hernia was general anesthesia administered. Further details regarding patients' demographics and anesthesia used are presented in Table 1.

The surgical procedure started with a ca. 3 cm large incision over the groin involved in the hernia protrusion and, depending on hernia type, was carried out as follows:

- In the case of indirect hernia, the external oblique fascia was opened and the hernia sac protruding from the deep ring identified (Fig. 2 A). After adhesiolysis and dissection of the hernia sac from the spermatic cord beyond the internal inguinal ring, the peritoneal protrusion emptied of its content was ligated and excised. Before returning the peritoneal stump into the abdominal cavity, a finger guided, or pad assisted, dissection of the peritoneal sheath from the posterior abdominal wall was

Table 1

Patient's demographics and anesthesia administered and follow up length.

Total patients enrolled	389	% 100
Gender		
Male/Female	343/46	Ratio 9/1
Age (median)		
46,16 years (range 18–84)		
BMI (median)		
27,43 (range 23–34)		
Anesthesia	Local 347 (89,2%)	General 42 (10,8%)
Follow up length 72/12 months		

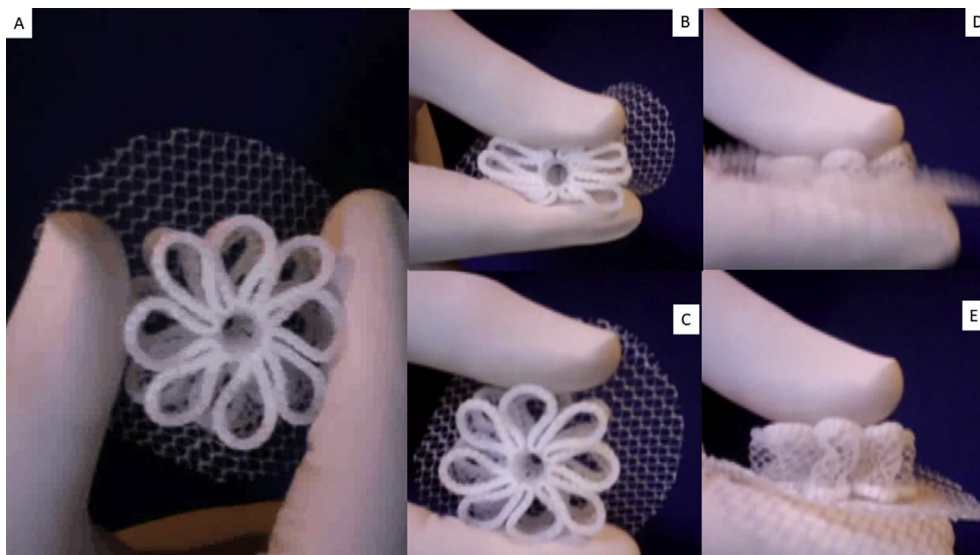


Fig. 1. A: 3D dynamic responsive implant and motile behavior in the case of longitudinal (B, C) as well as vertical compression (D, E).

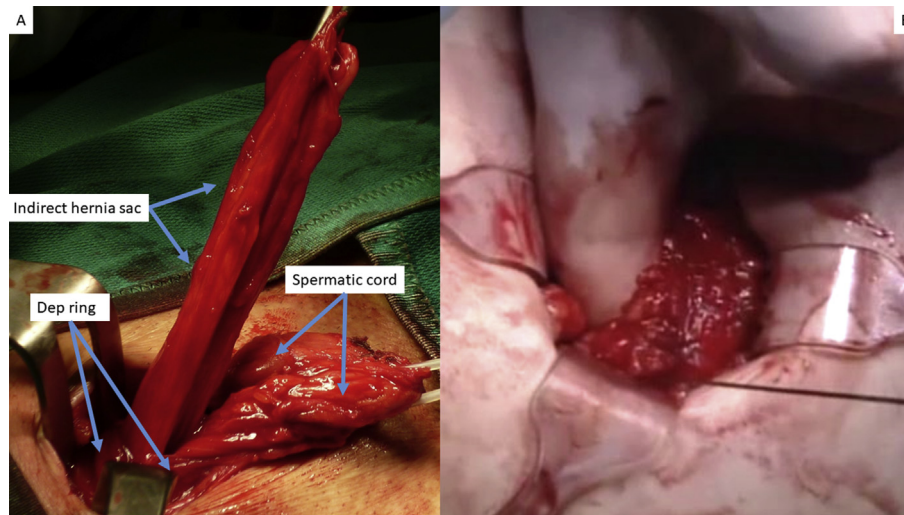


Fig. 2. A: large indirect inguinal hernia sac arises from the deep ring – B: After excision of redundant portion of hernia sac and returning the stump into the abdominal cavity, a finger guided dissection of the preperitoneal plane is carried out through the internal inguinal ring.

carried out (Fig. 2 B). This maneuver allowed to achieve a space large enough to accommodate the flat implant disk in the preperitoneal planes beyond the hernia opening (Fig. 3 A). In this way, the flat disk of the prosthesis interfaced the peritoneal sheath covering a large surface of the inguinal backwall. At this stage, the ProFlor™ implant was delivered into the patent internal ring. Due to its inherent radial expansion, the dynamic implant filled the opening without impairing the blood flow in the spermatic cord, which runs among the lamellas of the device (Fig. 3 B). (If needed, a forceps guided maneuver can be helpful to adjust the implant within the defect to ensure correct anatomical placement.)

- In the case of direct, external supravesical or combined hernia, the space for deploying the prosthesis and its flat disk was obtained by opening the transversalis fascia. Then, adhesiolysis of the protruding hernia content along the posterior inguinal backwall followed by means of a mounted pad and, finally, with the protrusion already returned to the abdominal cavity, the 3D

prosthesis was delivered to obliterate the hernial gap (Fig. 4A and B – Fig. 5A and B). Also in this case, the flat disk of the implant interfaced the peritoneal sheath covering a broad surface of the inguinal backwall.

- In the case of multiple ipsilateral inguinal hernia composed of double or multiple sacs arising from the internal ring, after ligation and excision of the sacs, the implant was delivered as specified for single indirect hernia (Fig. 6A and B). In the case of multiple ipsilateral hernias composed of one or multiple indirect plus one direct protrusion, or one direct plus one separated supravesical protrusion, the septum dividing the two hernias was dislodged or excised (Hocquet maneuver) to unify the protrusions at the discretion of the surgeon. Then, an adequately sized implant was positioned into the defects of the backwall unified in one single opening (Fig. 7A and B, C).

Regarding delivery of the implant, in the early phase of the investigation a proprietary delivery device was used for this scope.

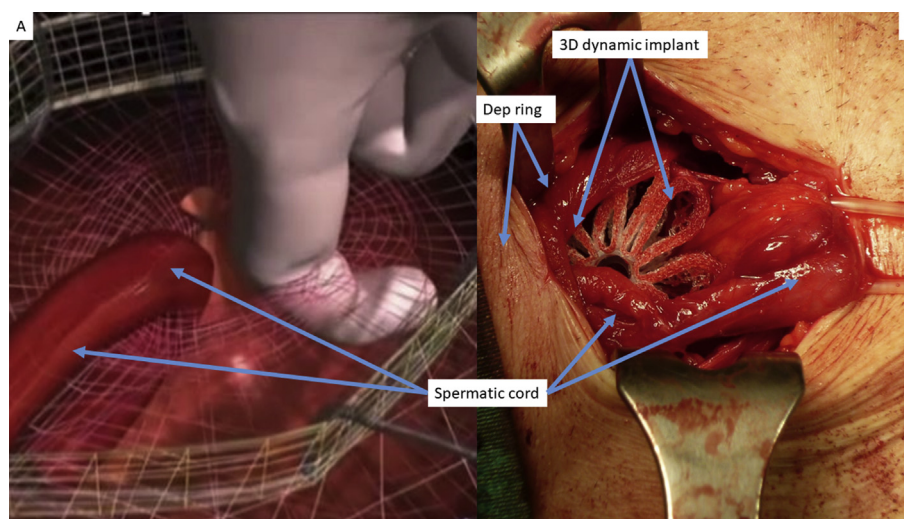


Fig. 3. A: schematic representation of the peritoneal dissection in the preperitoneal space beyond the internal ring before returning the stump of the hernia sac. - B: A 40 mm ProFlor™ implant has been delivered into the indirect hernia defect to fully obliterate the deep ring. The spermatic cord runs medially to the 3 D implant without compressive effects on the spermatic cord.

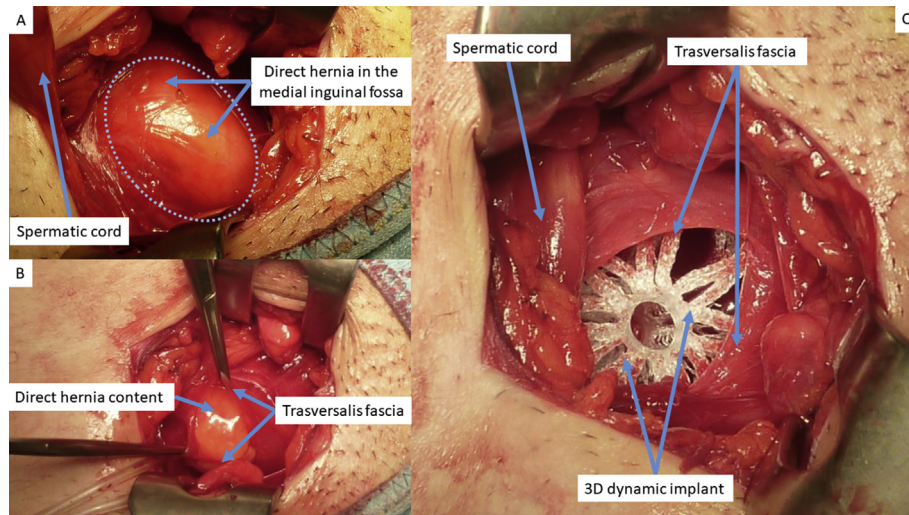


Fig. 4. A: direct inguinal protrusion covered by thin transversalis fascia. - B: Transversalis fascia has been opened, the hernia content tends to protrude through the breached transversalis fascia. - C: After broad dissection of the preperitoneal planes, a 40 mm ProFlor™ implant is delivered to obliterate the hernia opening which is partially covered by the transversalis fascia at its boundary.

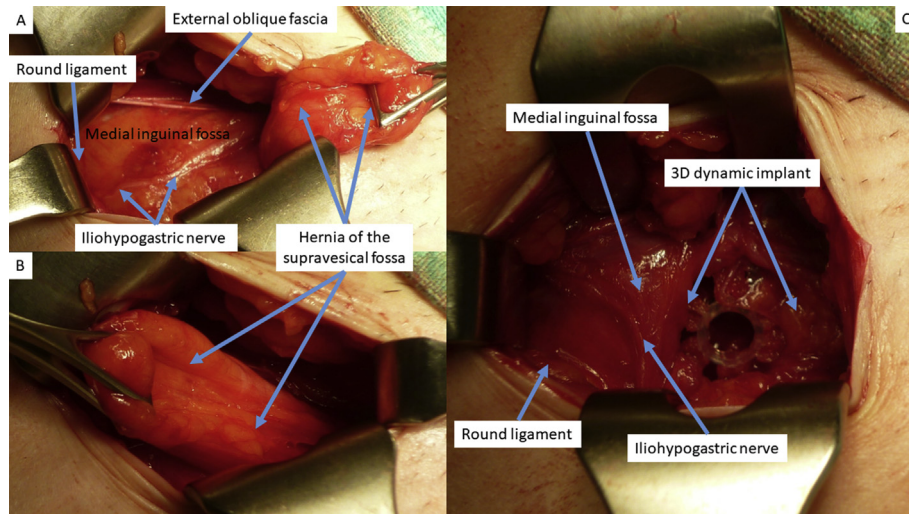


Fig. 5. A: a rare case of external hernia of the supravescical fossa in a female: the protrusion is dislodged medially to highlight the anatomy of the inguinal floor. - B: The hernia protrusion is dislodged laterally: preperitoneal fat is visible through a robust transversalis fascia. - C: After opening the hernia sac a broad dissection of the preperitoneal plane was carried out to allow deployment of one 25 mm ProFlor™ implant to obliterate the hernia opening.

Nevertheless, the maneuver was too time consuming as direct vision of the defect was hindered by the size of the delivery tool. Thus, the decision to deliver the implant into the defect by means of normal forceps was taken, thus significantly speeding up the procedure. The 3D implant was chosen to be always larger than the hernia opening, pushed over the defect into the preperitoneal space, then pulled back in order to interface the edges of the defect with those of the implant. No sutures, clips, tacks or glue were used to hold the prosthesis in place. To test the self-retaining behavior of the implant, all patients (except those operated under general anesthesia) were invited to repeatedly cough. This stress test was used to demonstrate the gripping strength of the implant also under expulsive movements. At this stage, the core of the procedure was completed. Suture of the external oblique fascia and closure of the subcutaneous layer then followed. The skin was closed with a total intradermal suture.

Postoperative follow-ups were carried out at 7 days, 15 days, then at 1, 3, 6, 12, 18 months and every subsequent year. The follow-

up also included physical examination and real-time ultrasound (US) scan to look for implant position.

3. Results

The 389 patients of the cohort were enrolled between January 2011–December 2017. All procedures were carried out in an outpatient surgery setting. Three patients were lost during follow up (one 32 months postop following a cardiovascular event, another at 43 months postop due to stroke and the third due to acute leukemia 54 months postop). The deaths were unrelated to the procedure. With regard to hernia types identified during the procedures, among the patients of the cohort, 148 (38.5%) suffered from indirect inguinal hernia, 58 (15.1%) had direct inguinal hernia, 40 (10.4%) combined hernia, and 27 (7%) external hernia of the supravescical fossa. A further 39 patients (10.1%) were operated for recurrent inguinal hernia (Table 2). A meticulous search for additional hernias arising from the same groin was considered as

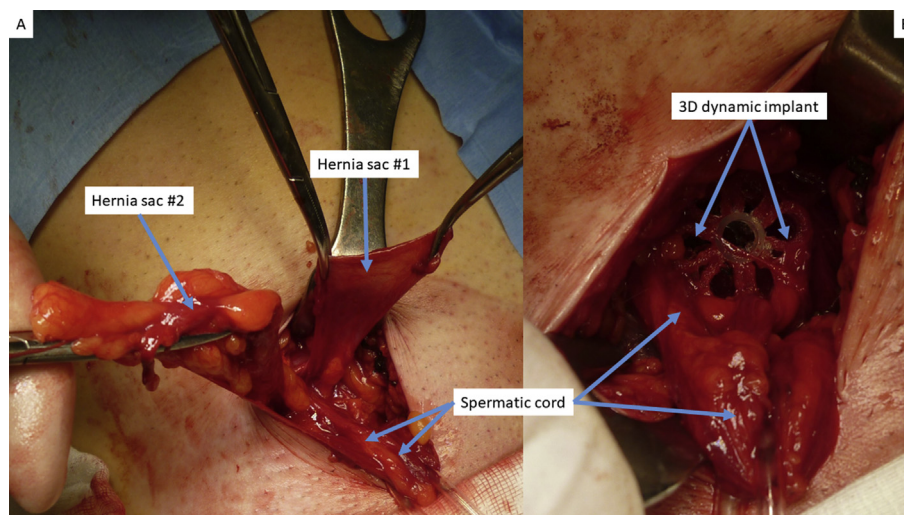


Fig. 6. A: double ipsilateral indirect protrusions arising from the deep ring after dissection of adhesions. - B: the internal inguinal ring fully obliterated by a 25 mm ProFlor™ implant. Of note, the spermatic cord runs laterally to the 3 D implant, no signs of compression of the spermatic cord vessels.

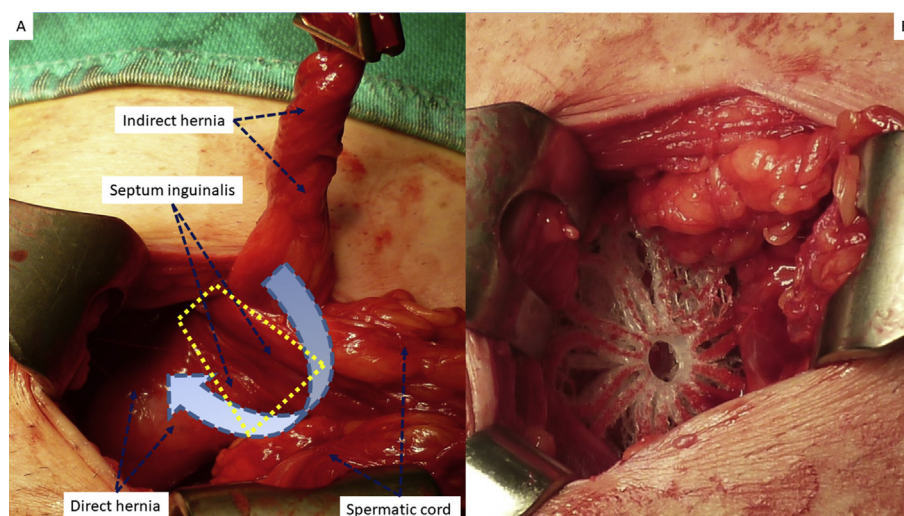


Fig. 7. Double ipsilateral hernias composed of one direct + one supravesical protrusion separated by a divisor septum. - A: After opening the transversalis fascia and dislodging the divisor septum laterally the hernias are unified. The merged protrusion will be pulled back into the abdominal cavity. - B: After returning the protrusion, the resulting single defect involving both the medial and the supravesical fossae is fully obliterated by one 40 mm ProFlor™ implant.

mandatory in all patients. A total of 37 patients (9.5%) with multiple ipsilateral inguinal hernias were identified, of which 16 were multiple indirect hernias with all protrusions arising from the internal ring. An additional 20 multiple protrusions pertinent to this subgroup were composed of one direct plus 1 or multiple indirect hernia separated by a divisor septum. One further multiple ipsilateral protrusion was composed of one supravesical and one direct

hernia separated from each other by a divisor septum. The divisor septum of the inguinal backwall, a typical occurrence in multiple protrusion types, was excised in 17 patients to unify the two protrusions in a single one. In three cases, the divisor septum was so thin that the merger of the defects was achieved by dislodging the septal arrangement and tunneling the direct hernia protrusion under the septum. In another patient, the divisor septum showed a thick muscular arrangement. In this case, the septum of the backwall was not excised and the defects could be obliterated by positioning two 25 mm large implants in each of the two separate defects. Details on hernia types identified during the surgical procedures are described in Table 2. Concerning the implant sizes used, 181 hernia defects were obliterated with the 25 mm prosthesis and 208 with the 40 mm implant. The surgical procedures were safely carried out in a time ranging from 20 to 40 min in the case of primary hernia repair, 40–60 min in the case of recurrent hernias.

Regarding postoperative complications, the occurrence of hematic skin suffusion in the early postoperative stage was not

Table 2
Hernia types identified during the surgical procedures.

Hernia types		
Indirect	168	43,1%
Direct	69	17,8%
Combined	44	11,3%
Double or multiple ipsilateral	37	9,5%
Supravesical	29	7,5%
Recurrent	42	10,8%
Total	389	100%

considered a complication. The most frequent adverse event was seroma that affected 15 patients (3.8%) in the early postoperative stages. Three of these seromas needed needle aspiration, the remaining were managed with conservative therapy and US check-ups. Three patients suffered from postoperative hematoma of which one was resolved with needle aspiration. One case of postoperative testicle retraction was reported after 4 months in a patient who underwent recurrent hernia repair. Four recurrences were reported, of which three were small forgotten hernias which had not been detected during primary repair. No incidence of postoperative infection, discomfort or chronic pain was reported among the studied patient cohort. Return to normal activities occurred between the 4th and 10th postoperative day (median 6 days). Details of postoperative complications are shown in Table 3.

Concerning postoperative pain assessed with the VAS scoring scale, the results were promising: after discharging the patient the same day of the operation the pain score was close to 3 VAS points. However, after 7 days the VAS score revealed almost no pain. Starting from 2 weeks postoperative no more pain was reported, even under loading movements (Table 4).

4. Discussion

Despite the high volume of inguinal hernia repair procedures, many adverse events still affect the results of the surgical treatment of this widespread disease. Apart from the almost obsolete pure tissue repair carried out by the open anterior approach, the main repair methods involve the deployment of flat meshes with the aim

to reinforce the inguinal floor [13,16,21]. Mesh repair is nowadays mainly accomplished via the open anterior or laparoscopic posterior approach. In both cases, some procedural aspects do not appear to be in line with the physiology and kinetics of the groin. For example, the need for fixation of the implanted mesh, in the last few decades, has represented a continuous source of debate among scientists. Mesh fixation, with sutures in open, or with tacks in laparoscopic, repair seems controversial if the dynamic feature of the inguinal area is taken into consideration. Point sutures or screws applied in a mobile and highly sensitive muscular surround contrasts with the dynamic behavior of the inguinal area. Most reported postoperative complications, such as tissue tear, bleeding, hematomas, mesh dislocation, discomfort or chronic pain, are related with mesh fixation [22–24]. Even the highly expensive fibrin glue fixation, causing additional inflammatory reaction to be reabsorbed and fully degraded within two weeks, does not appear to be an effective fixation method [25,26].

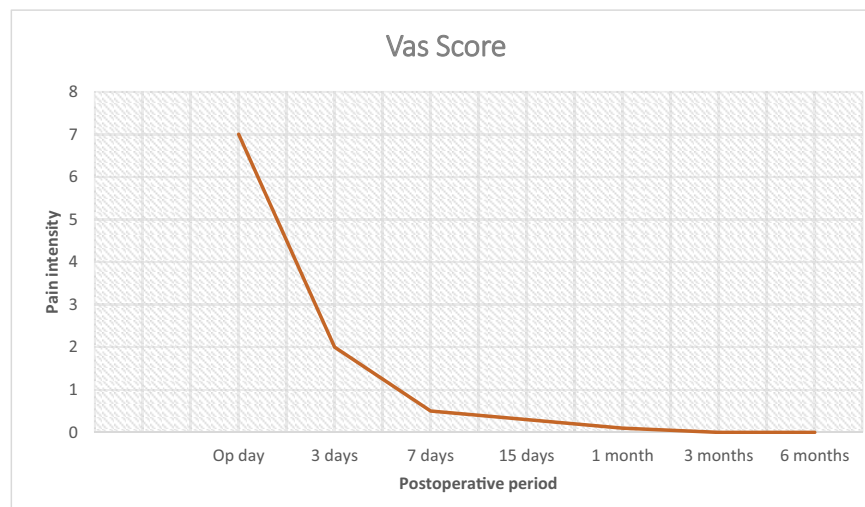
Further concerns derive from the procedural approach, typical in open and laparoscopic flat mesh repair, to simply cover, not obliterate, the inguinal defect. Above all, in the case of open indirect hernia repair, the defect remains patent, while in direct hernia repair the lifting of a weak, often degenerated, fascia transversalis does not always assure effectiveness of the suture. A variant of this approach is the so-called plug and mesh repair carried out with introduction of a static plug into the defect [21]. Nevertheless, two problems arise in this case: first, to avoid migration, the plug must be fixated to the myotendineal surround, a further hindrance to groin movements and possible source of complications. Secondly, within a few months, the plug shrinks up to 60% often leaving the defect partially patent. In literature, no attempts to obliterate the patent hernial gap are described for laparoscopic inguinal hernia repair [27,28]. Ineffective management of the patent defect seems to prelude postoperative discomfort and recurrence if the visceral content restarts to impact against a weakened inguinal barrier.

A further controversial subject in prosthetic inguinal hernia repair is the biologic response of flat meshes: a stiff fibrotic incorporation into the implant fabric. Mesh incorporation by a hard, fibrotic plaque produces shrinkage of the prosthesis that, with time, can result in de-coverage of the groin's backwall [27,28]. Furthermore, two other phenomena can develop after this stiffened compound is established: discomfort due to rubbing of the

Table 3
Results of the procedures.

Complications	Numbers	Incidence
Seroma	15	3,8%
Hematoma	3	0,9%
Sepsis/Abscess	0	0%
Recurrence/forgotten hernia	4	1%
Testicle retraction	1	0,2%
Discomfort	0	0%
Chronic pain	0	0%
Total	23	5,9%
Return to normal activity (days)	6 (median)	Range 4 - 10

Table 4
Postoperative pain intensity.



stiffened compound - scar plate and shrunken mesh - during movements, which is often perceived by patients, even in a long term postoperative phase. An additional adverse event may be the more feared chronic pain caused by incorporation of one or more inguinal nerves among the uncontrolled fibrotic proliferations of the flat mesh [10,22–24].

However, none of the hernia repair methods take the pathogenesis of the disease into consideration. Through several recent studies, it has been demonstrated that inguinal hernia is a degenerative disease with the distinctive trait of chronic compressive damage [4–8]. Consequently, regeneration of the degenerated groin tissue should be the target of the treatment. Fibrotic scar ingrowth within flat meshes does not resemble a regenerative, but rather a regressive, response similar in all aspects to foreign body reaction. This response is quite far from healing a degenerative disease through restoring the missing tissue components.

Summarizing, in an analysis of the current state-of-the-art inguinal hernia repair, a wide spectrum of incongruences arises:

- Static repair concept with passive and motionless prosthetics, in managing a disease affecting a highly dynamic surround.
- Fixation of prosthetic devices upon the myotendineal structure of one of the most motile and sensitive parts of the body - the groin.
- Simple coverage of the hernial gap. Defect patent, no obliteration. Risks of mesh dislocation in open and mesh invagination in laparoscopic repair.
- Uncontrolled regressive biologic response to the prosthetic devices leading to mesh shrinkage and potential de-coverage of the defect. Nerve entrapment in fibrotic proliferation is also possible.
- Disregard, or even unawareness of the pathogenesis of hernia disease

The points raised above represented the background for a deeper analysis carried out with the aim of achieving an effective, ameliorating, concept change in inguinal hernia repair. Currently, the concept of reinforcing the groin with static and fixated implants established more than half a century ago remains, albeit with slight modifications of procedural steps or implant fabric. However, there is an unacceptable amount of frequent and specific complications.

Following these considerations, a real concept change in inguinal hernia repair should include respect of the physiology of the groin and its motile feature. There is also the belief that inguinal hernia disease can be properly managed having better knowledge of its genesis, the significance of which has been for too long underestimated.

Starting from these premises, a series of interconnected translational investigations was undertaken. This involved the detection of functional modifications of groin anatomy, dynamics and physics of the abdominal wall, physiopathology and histology of the herniated groin, histological control studies in living patients and cadavers with/without hernia, pathogenetical investigations based on modifications of functional anatomy and related histological changes [4–8,29–31]. The development of the 3D dynamic compliant implant was the result of these studies. The ProFlor™ prosthesis was then tested through a long term experimental attempt in a porcine animal model whose results exceeded the best expectations in terms of surgical reliability and biological compatibility [20]. This novel prosthetic device seems to possess all features for a comprehensive treatment of inguinal hernia disease:

- It is designed to be self-retaining. Due to its inherent centrifugal expansion no fixation is needed

- It does not cover but fully and permanently obliterates the hernia defect
- Physiologic and dynamic integration: it moves in synchronization with the groin – not perceivable by patients
- Probiotic response: it induces ingrowth of typical tissue elements of the inguinal area
- It produces a well vascularized fleshy structure, re-establishing the inguinal barrier injured by the disease

The outcome of all these positive features seem to be adequately highlighted in the results evidenced above and explained herewith.

Firstly, the surgical procedure can be carried out quickly and safely with reduced risks of intraoperative injuries. Complete obliteration of the defect through the centrifugal expansion of the ProFlor™ implant and the resulting self-retaining effect makes any kind of fixation superfluous. Eliminating the need for implant fixation avoids wasting time, as well as intra and postoperative complications related to point sutures in the inguinal surround. This is also positive in terms of reducing postoperative pain.

Dynamic compliance, as well as the stability of the implant, firmly lodged into the defect, can be immediately tested in all patients operated in local anesthesia. The motile behavior of the 3D implant, placed in the deepest section of the inguinal floor, is significant for the imperceptibility of the prosthesis by patients, also long term. This is radically different compared to the deployment of conventional motionless and fixated meshes whose point sutures or tacks hinder inguinal movements during motion.

A further innovative and proprietary feature evidenced in animal and human studies relates to the ingrowth of specific abdominal wall tissue within the 3D implant starting from the early stage postop. A series of scientific reports well highlights the behavior of the dynamic prosthesis that acts as a regenerative scaffold leading to the incorporation of newly formed mature vessels, muscle fibers nerves and well hydrated connective tissue within the implant [20,32,33]. A comparative study concerning the quantitative and qualitative assessment of the biologic response in conventional static prostheses and in 3D dynamic responsive implants appears to further confirm the promising results of the newly designed 3D prosthetic device [33]. In conventional static meshes, a constant histological finding has been the ingrowth of a typically regressive fibrotic scar plate showing limited vascular structures devoted to supporting a long lasting inflammatory infiltrate. No development of high specialized structures such as myocytes or nervous elements can be detected in static meshes. On the contrary, in the ProFlor™ implant all typical elements constituting the inguinal wall could be detected: veins, arteries and nerves complete in all constituents together with a large amount of newly formed fully matured myocytes (Fig. 7A). Such a feature could be envisaged as the finalization of the regenerative effort and seems to confirm the desired effect for a device intended to effectively resolve degeneration induced by the disease: a pathogenetical consequent biological response.

In the initial stage of implant development, this regenerative feature was unexpected. After experimental trials in a porcine model, the probiotic implant response was surprisingly evidenced [20]. One hypothesis may explain the very different biological behavior of the two types of implants both made of the same polypropylene material: the conventional flat mesh and ProFlor™. The only evident dissimilarity between the tools is the implant shape. The flat arrangement of conventional meshes positioned to cover the inguinal area, being static, motionless and passive, is not intended to interact with the kinetics of the inguinal structures. This explains the foreign body reaction with development of a stiff scar plate, a typical result of this type of prostheses. On the other hand, the proprietary shape of the 3D implant positioned to

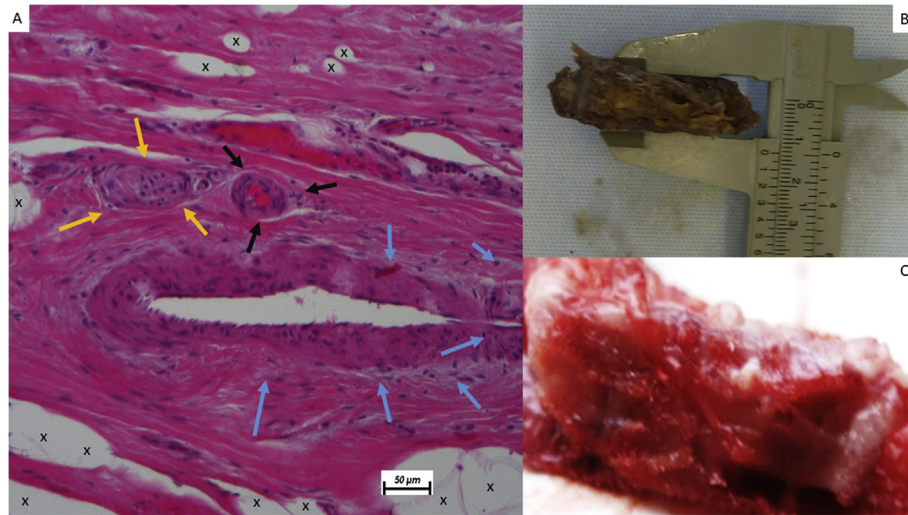


Fig. 8. A: 40 mm sized ProFlor™ split in the midline excised from the groin of porcine model 6 months postop. The implant fabric, covered by the newly ingrown fleshy tissue, is no longer recognizable. The fleshy compound resembles a viable muscular barrier in all aspects. B: 40 mm ProFlor™ implant removed 3 years postop, due to recurrence. The implant had been already fixed for 24 h in 10% phosphate-buffered formalin to be histologically examined. Caliper assessment shows a thickness of circa 1 cm. - C: Biopsy specimen of the 3D dynamic implant shown in B: among the implant fibers (x) a large vein (blue arrows), a well-formed artery (black arrows), one nerve complete of myelin sheath and mature axons in a context of many myocytes are detectable. EE 100X.

permanently obliterate a defect in the highly motile inguinal backwall, moves in synchrony with the groin thanks to its dynamic behavior. This steady compliance to movements of ProFlor™ allows stretching and relaxing of the connective fibers ingrown in the device. The continuous movements impede loss of water content avoiding the stiffening of the connective tissue incorporated in the implant fabric. The cyclic motion to which the prosthesis is subjected seems to attract growth factors typical of this specific anatomical site: the abdominal wall. The result is the re-establishing of a thick, fleshy inguinal barrier. This was seen in implants excised from porcine models during the experimental stage, as well as in the sole implant removed for recurrence in the whole patient cohort 3 years postop (Fig. 8A and B, C). The sequence of phenomena and the contribution of growth factors should be subject of further scientific investigations. Nevertheless, in light of the histological evidence, the hypothesis raised sounds consistent.

The incidence of recurrences deserves a separate note: 1% is an excellent result. Nevertheless, of the four recurrences reported, three involved forgotten protrusions undetected during primary repair. All three cases occurred in the early period of the clinical study and were of great importance for a reflection on how to avoid this particular type of mishap. Being the dynamic hernia repair a selective defect obliteration, overlooking a small hidden protrusion of the backwall makes the appraisal of larger protrusions possible, with time, which evidently is not a recurrence, but the development of an additional, previously undetected, hernia. Following these experiences, this issue was scientifically investigated with specific studies that demonstrated an overall 10% incidence of multiple ipsilateral inguinal protrusions. This occurrence is confirmed by other, although in limited amount, scientific reports [34–38]. Consequently, the meticulous search of hidden additional protrusions during inguinal hernia repair procedures is considered as mandatory for successful surgical treatment with the 3D dynamic implant.

An effective limitation in the use of this 3D implant concerns the maximum defect size that can be obliterated with the ProFlor™ implant. Currently, defects larger than 37 mm are not indicated for repair with the 40 mm implant. However, in our experience more than 90% of all inguinal defects are smaller than 37 mm. Nevertheless, the development of larger implants is under consideration.

An apparent limitation of the use of the 3D dynamic responsive implant seems to be the sizes of the device. At first glance, surgeons may perceive the 3D prosthesis as too bulky. This perception probably depends on previous widespread conventional surgical treatment with thin implants and is fully comprehensible. However, we are facing two different concepts of inguinal hernia repair: the conventional reinforcement of inguinal wall exerted by thin, flat prostheses incorporated by a hard, fibrotic plaque, against restoring the degenerated barrier of the inguinal backwall by means of a regenerative scaffold: the 3D dynamic implant. The thickness of the 3D prosthesis has been specifically designed to be comparable in width to the muscular barrier of the inguinal area. The incorporation of newly formed fleshy tissue within the 3D prosthesis produces a viable barrier that can effectively counteract the impact of the abdominal viscera. In this regard, Fig. 8A and B & C could help in further clarifying the matter.

In addition, the need for dissecting the peritoneal sheath to deploy the preperitoneal flat disk of the implant could theoretically be intended as a source of concern, although the peritoneal dissection from the posterior inguinal backwall with a finger guided maneuver or with the help of a pad can be carried out quickly and safely. No case of intraoperative mishaps or injury of the inferior epigastric vessels were reported performing this task.

However, a factual limitation of this study arises from possible bias deriving from the correspondent author, who is the developer of the implant and the related surgical technique. Nevertheless, the evidence demonstrated and discussed in the report seems to adequately balance said perception.

5. Conclusions

The described features probably help in understanding why the postoperative outcomes of the dynamic hernia repair carried out with the 3D implant ProFlor™ were so encouraging. As an example, the low pain scores reported in the early postoperative phase and the absence of pain starting from two weeks postop seem to be a direct consequence of the fully fixation free implant deployment as well as its physiological integration within the inguinal area. In this regard, a positive effect probably derives from the proprietary skin closure technique without external stitches penetrating the highly

sensitive inguinal skin [34]. The reduced overall incidence of adverse events represents one of the positive effects of this type of inguinal hernia repair. However, the quality of the postoperative complications is deemed of greater significance. Aside from the low number of seromas and hematomas, mostly managed conservatively, the absence of complications that frequently affects the late postoperative stages of conventional hernia repair techniques stands out: discomfort and chronic pain. These adverse events, hard to manage and prelude to a worsened quality of life, were totally lacking among the studied patient cohort. This seems to be a direct effect of three features: real fixation free deployment technique, physiological integration and probiotic biological response of the implant.

Ethical approval

The ethic approval has been granted by the Ethic Commission of the Medical Board of the Land Hessen/Germany. Ref. FF137/2012.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

Giuseppe Amato study conception and drafting of manuscript. Giorgio Romano designed the study. Luca Cicero and Eliana Gulotta data acquisition. Thorsten Goetze analysis and interpretation of data. Antonino Agrusa and Pier Giorgio Calò critical revision of manuscript.

Conflict of interest statement

The corresponding author is the developer of the implant and related surgical technique. All other authors have no conflict of interest.

Guarantor

Prof. Giuseppe Amato.

Research registration number

Name of the registry: Research Registry.
Unique Identifying number or registration ID: researchregistry4998.

Hyperlink to the registration (must be publicly accessible):
<https://www.researchregistry.com/register-now#home/registrationdetails/5d20654a48b066001018c855/>

Human and animal right

The study including human participants has been performed in accordance with the ethical standards of the.

Declaration of Helsinki and its later amendments.

Informed consent

Informed consent was obtained from all patients prior to all surgical procedures.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2019.10.008>.

References

- [1] Friedman DW, Friedman DW, Boyd CD, Greco RS, Boyarsky AH, Mackenzie JW, et al. Increases in type III collagen gene expression and protein synthesis in patients with inguinal hernias. *Ann Surg* 1993;218(6):754–60.
- [2] Klinge U, Binnebösel M, Mertens PR. Are collagens the culprits in the development of incisional and inguinal hernia disease? *Hernia* 2006;10(6):472–7.
- [3] Pans A. Biochemical study of collagen in adult groin hernias. *J Surg Res* 2002;95(2):107–13.
- [4] Amato G, Marasa L, Sciacchitano T, Bell SG, Romano G, Gioviale MC, et al. Histological findings of the internal inguinal ring in patients having indirect inguinal hernia. *Hernia* 2009;13:259–62.
- [5] Amato G, Ober E, Romano G, Salamone G, Agrusa A, Gulotta G, et al. Nerve degeneration in inguinal hernia specimens. *Hernia* 2011;15:53–8.
- [6] Amato G, Romano G, Salamone G, Agrusa A, Saladino VA, Silvestri F, et al. Damage to the vascular structures in inguinal hernia specimens. *Hernia* 2012;16:63–7.
- [7] Amato G, Agrusa A, Romano G, Salamone G, Gulotta G, Silvestri F, et al. Muscle degeneration in inguinal hernia specimens. *Hernia* 2012;16(3):327–31.
- [8] Amato G, Agrusa A, Romano G, Salamone G, Cocorullo G, Mularo SA, et al. Histological findings in direct inguinal hernia. *Hernia* 2013;17(6):757–63.
- [9] Kingsnorth A, LeBlanc K. Hernias: inguinal and incisional. *Lancet* 2003;362:1561–71.
- [10] Kim-Fuchs C, Angst E, Vorburger S, Heibling C, Candinas D, Schlumpf R. Prospective randomized trial comparing sutured with sutureless mesh fixation for Lichtenstein hernia repair: long-term results. *Hernia* 2012;16(1):21–7.
- [11] EU Hernia Trialist Collaboration. Mesh compared with nonmesh methods on open groin hernia repair. Systematic review of randomized controlled trial. *Br J Surg* 2000;87:854–9.
- [12] Read RC. Recent advances in the repair of groin herniation. *Curr Probl Surg* 2003;40(1):13–79.
- [13] Amid PK. Lichtenstein tension-free hernioplasty: its inception, evolution, and principles. *Hernia* 2004;8:1–7.
- [14] Amid PK, Shulman AG, Lichtenstein IL, Hakakha M. Biomaterials for abdominal wall hernia surgery and principles of their applications. *Langenbecks Arch Chir* 1994;379(3):168–71.
- [15] Klosterhalfen B, Klinge U, Schumpelick V. Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. *Biomaterials* 1998;19:2235–46.
- [16] Klosterhalfen B, Junge K, Klinge U. The lightweight and large porous mesh concept for hernia repair. *Expert Rev Med Devices* 2005;2:103–17.
- [17] Amato G, Agrusa A, Romano G. Fixation-free inguinal hernia repair using a dynamic self-retaining implant. *Surg Technol Int* 2012;30(XXII): 22/17.
- [18] Amato G, Romano G, Agrusa A, Cocorullo G, Gulotta G, Goetze T. Dynamic inguinal hernia repair with a 3d fixation-free and motion-compliant implant: a clinical study. *Surg Technol Int* 2014;24:155–65.
- [19] Campanelli G, Morlacchi A, Bruni PG, Cavalli M. 3D dynamic anterior repair: ProFlor technique in Campanelli: inguinal hernia surgery. Springer; 2017. p. 43–8.
- [20] Amato G, Lo Monte AI, Cassata, Damiano G, Romano G, Bussani R. A new prosthetic implant for inguinal hernia repair: its features in a porcine experimental model. *Artif Organs* 2011;35(8):E181–90.
- [21] Rutkow IM, Robbins AW. Mesh plug hernia repair: a follow-up report. *Surgery* 1995;117:597–8.
- [22] Amid PK. Causes, prevention, and surgical treatment of postherniorrhaphy neuropathic inguinodynia: triple neurectomy with proximal end implantation. *Hernia* 2004;8:343–9.
- [23] O'Dwyer PJ, Kingsnorth AN, Mohillo RG, Small PK, Lammers B, Horeysee G. Randomized clinical trial assessing impact of a lightweight or heavyweight on chronic pain after inguinal hernia repair. *Br J Surg* 2005;92:166–70.
- [24] Aasvang E, Kehlet H. Surgical management of chronic pain after inguinal hernia repair. *Br J Surg* 2005;92:795–801.
- [25] Katkhouda N, Mavor, Friedlander MH, Mason RJ, Kiyabu M, Grant SW, et al. Use of fibrin sealant for prosthetic mesh fixation in laparoscopic extraperitoneal inguinal hernia repair. *Ann Surg*. Jan 2001;233(1):18–25.
- [26] Negro P, Basile F, Brescia A, Buonanno GM, Campanelli G, Canonico S, et al. Open tension-free Lichtenstein repair of inguinal hernia: use of fibrin glue versus sutures for mesh fixation. *Hernia* 2011;15(1):7–14. Feb.
- [27] Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. *Hernia* 1997;1:15–21.
- [28] Klinge U, Klosterhalfen B, Muller M, Ottinger AP, Schumpelick V. Shrinking of polypropylene mesh in vivo: an experimental study in dogs. *Eur J Surg* 1998;164:96.
- [29] Amid PK. Shrinkage: fake or fact? In: Schumpelick V, Nyhus LM, editors. *Meshes: benefits and risks*. Springer Berlin; 2004.
- [30] Amato G, Sciacchitano T, Bell SG, Romano G, Cocchiara G, Lo Monte AI, et al. Sphincter-like motion following mechanical dilation of the internal ring during indirect inguinal hernia procedure. *Hernia* 2009;13:67–72.

- [31] Amato G, Agrusa A, Rodolico V, Puleio R, Di Buono G, Amodeo S, et al. Combined inguinal hernia in the elderly. Portraying the progression of hernia disease. *Int J Surg* 2016;(Suppl 1):S20–9.
- [32] Amato G, Calò P, Rodolico V, Puleio R, Agrusa A, Gulotta L, et al. The septum inguinalis: a clue to hernia genesis? *J Investig Surg* 2018;31:1–9. Oct.
- [33] Amato G, Romano G, Puleio R, Agrusa A, Goetze T, Gulotta E, et al. Neomyogenesis in 3D dynamic responsive prosthesis for inguinal hernia repair. *Artif Organs* 2018;42(12):1216–23. Dec.
- [34] Amato G, Romano G, Agrusa A, Marasa S, Cocorullo G, Gulotta G, et al. Biologic response of inguinal hernia prosthetics: a comparative study of conventional static meshes versus 3D dynamic implants. *Artif Organs* 2015;39(1). Jan.
- [35] McQueeney A. Multiple sacs in inguinal hernia. *Ann Surg* 1926;83(1):81–3.
- [36] Ekberg O, Lasson A, Kesek P, Van Westen D. Ipsilateral multiple groin hernias. *Surgery* 1994;115:557–62.
- [37] Mayank J, Shashi K, Bimalendu S, Om T. Ipsilateral occult hernias during endoscopic groin hernia repair. *J Minimal Access Surg* 2008;4(2):44–7.
- [38] Amato G, Agrusa A, Romano G. Multiple ipsilateral inguinal hernias: more frequent than imagined, if undetected source of discomfort, pain, and Re-interventions. *Surg Technol Int* 2014;25:130–5.