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ORIGINAL ARTICLE

Introducing a true minimally invasive meshless and dissectionless anchoring system for pelvic organ prolapse repair

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Abstract
Introduction and hypothesis The objective was to demonstrate the biomechanical properties, feasibility, and potential advantages over conventional techniques of this new anchoring device, NeuGuide™.
Methods We evaluated the pull-out forces required to pull the NeuGuide™ anchor elements from a uniform porcine ligament and a cadaver ligament. We also evaluated the function of the NeuGuide™ and the characteristics of the device for the establishment of verification evidence ensuring the reliability and feasibility of the device. We also evaluated the safety and performance of the NeuGuide™ procedure in female cadavers by palpating the sacro-spinous ligament in real time. We assessed the ability to deploy and fixate the anchor to the sacro-spinous ligament and to stitch the sutures from both sides of the vaginal apex to the cervix, without damaging the surrounding structures.
Results All 12 anchors were inserted into the porcine ligament and the cadaver sacro-spinous ligaments successfully (mean pull-out force 34.13±4.32 and 35.68±9.28 respectively). None of the measured forces were below 20 N. No statistically significant difference was noted in the pull-out forces between the porcine and the cadavers (p=0.60), between the two cadavers (p=0.19) and between the right and left sacro-spinous ligaments. No abnormalities or malfunctions were noted in the functional performance of the device. Upon laparotomy, dissection of the cadavers revealed that the sacro-spinous ligaments were reached safely with no damage to the surrounding organs and tissues.
Conclusions This novel anchoring device (NeuGuide™) is aimed at facilitating a durable, easy, and short procedure for sacro-spinous ligament fixation with hypothetically fewer operative complications.

Keywords Anchoring device · NeuGuide™ · Sacro-spinous ligament fixation · Biomechanical properties

Introduction

Apical prolapse is defined as the descent of the apex of the vagina into the lower vagina, up to or beyond the hymeneal ring. The apex can be either the uterus and cervix, the cervix alone, or the vaginal vault, depending upon whether the woman has undergone hysterectomy. The classification of prolapse according to the separate compartments is arbitrary, as the vagina is a continuum and the prolapse of one compartment is often associated with the prolapse of another [1].

Loss of apical support is usually present in women with advanced and symptomatic prolapse that extends beyond the hymen. Women may present with symptoms of anterior, posterior, central prolapse or any combination of these. Clinical manifestations include a bulging sensation or vaginal pressure, and urinary, defecatory or sexual dysfunction [2]. There is a growing understanding that adequate vaginal apex support is essential for a durable surgical repair in women with

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advanced prolapse [3]. Moreover, surgical correction of the anterior and posterior walls may fail unless the apex is adequately supported [4].

Pelvic organ prolapse (POP) is a common problem in women and often requires surgical correction. In the USA, about 200,000 women undergo surgery for prolapse correction every year [5]. The lifetime risk to a woman of undergoing a surgical procedure for the correction of pelvic floor dysfunctions is 11–12.6 %. The risk of POP surgery was found to increase progressively until the age of 71–73 years, with an annual risk of 4.3 per 1,000 women [6]. Among these women, there is a close to 30 % risk of re-operation owing to the failure or prolapse of another compartment [7].

There is a wide variety of surgical treatments available for prolapse, which indicates that there is a lack of consensus with regard to the optimal surgical approach [3, 8].

Transvaginal sacro-spinous ligament fixation (SSLF) was shown to have shorter operating time, fewer wounds, quicker recovery to daily activities, and was cheaper than abdominal sacro-colpopexy [9]. Moreover, the vaginal approach facilitates the concomitant correction of other vaginal defects as well. Because of a high risk for ureteral injury, the sacrospinal ligament (SSL) is preferred to the uterosacral ligament as the fixation point [10]. However, transvaginal anchoring or placement of the fixation sutures to the SSL through a deep, narrow space is technically challenging and potentially dangerous. Indeed, numerous surgical adjuncts for SSL anchoring or suture placement have been introduced over the years, with no one device proven to be superior to others [11–16]. What all these techniques have in common is the need for deep vaginal dissection to gain safe access to the SSL. Many SSLF operations involving mesh implants have been criticized by the FDA for causing severe and frequent adverse effects [17].

We have developed a new anchoring device with the intention of providing a minimally invasive, dissectionless approach to SSLF. This device enables the surgeon to perform a pelvic centro-apical support operation with no mesh implants, using just suturing materials. We hypothesize that this new device might show good biomechanical properties and feasibility and that it might enable us to discuss potential advantages.

Our study integrated the testing of the device on porcine ligaments and later on female cadavers. The aim of this preliminary study is to demonstrate the biomechanical properties, feasibility, and potential advantages of this new device, NeuGuide™, by objectively measuring its anchoring performance on porcine ligaments and on cadavers.

Materials and methods

There were three main purposes of this study. First, we aimed to evaluate the pull-out forces required to pull the NeuGuide™ anchor elements from a uniform porcine ligament and a cadaver ligament. Second, we sought to evaluate the function of the NeuGuide™ and the characteristics of the device for the establishment of verification evidence, ensuring reliability and feasibility. Third, we wanted to evaluate the safety and performance of the NeuGuide™ device procedure in female cadavers by assessing the identification of the SSL, in real time, by palpation, the ability to deploy and fixate the anchor to the SSL, and to stitch the two sutures from both sides of vaginal apex to the cervix, without damaging the surrounding structures.

Device description

We developed a novel device, the NeuGuide™. This new product is designed to enable apical central support for the uterine cervix without the need for both vaginal dissection and mesh implants in patients with a central compartment defect that requires suspension. The NeuGuide™ device comprises two main elements: an anchor unit and a delivery system (Fig. 1). The delivery system enables the insertion, guidance, and deployment of the anchor element. The anchor unit of the device is designed as a sharp needle point nitinol harpoon, enabling piercing through the vaginal layers and the ligament. The anchor is deployed and placed with the use of an applicator. The anchor incorporates a surgical suture at its distal end, which, following its deployment, enables fixation and the continuation of the surgical procedure as intended for the repair process. A thimble is an accessory to the device that can be used as an introducer for better handling of the NeuGuide™ (Fig. 2).

The anchor penetration diameter is 2.0 mm. Once deployed (once it has passed the SSL), the wings open to 4.0 mm. The work channel length is 120 m (this limits the anchor penetration depth beyond the ligament to avoid injury). The device shaft diameter is 2.5 mm and its length 285 mm. The suture length is 70 cm and the work channel is designed to fit all sizes (self-adjusting).

The applicator includes two concentric hollow shafts. The outer shaft constrains the anchor wings from being deployed. Once the button is pressed, the inner shaft pushes the anchor

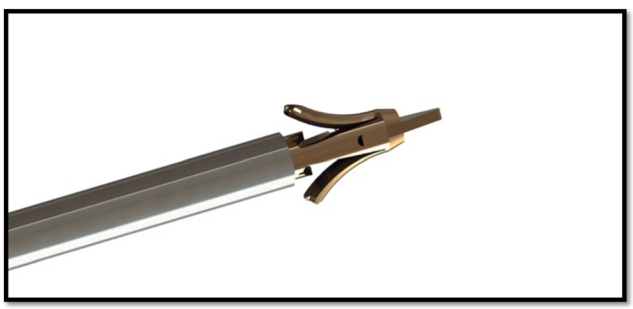

Fig. 1 The NeuGuide™ anchor elements

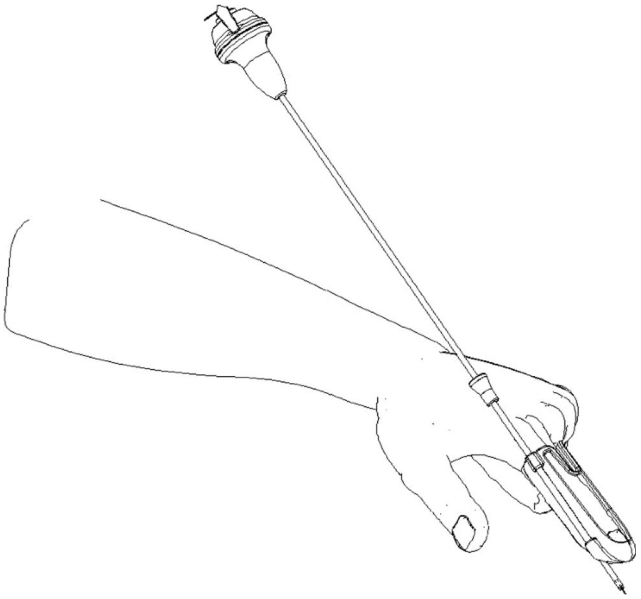

Fig. 2 A schematic drawing of an accessory referred to as the "Thimble" facilitates the insertion of the NeuGuide™ delivery system (with the anchor at its distal end) through it into the desired location on the ligament

distally and allows the wings to deploy. The applicator is equipped with a safety latch that protects the button, to avoid undesired deployment.

A 10-step surgical procedure

1. The NeuGuide™ device is mounted on the right index finger.
2. The right ischial spine and the SSL are palpated.
3. The index finger is stabilized intimately to the mid SSL.
4. The harpoon is launched.
5. There is testing for adequate anchoring.
6. A 1-cm, shallow, high, posterior colpotomy is performed.
7. A suture is mounted on a virgin needle.
8. A good bite of the cervix is taken between the entering point under the vaginal mucosa and out through the posterior colpotomy.
9. The previous steps are repeated on the left-hand side and the suture is tied appropriately.
10. The colpotomy is closed.

Animal study

A single 67-kg porcine specimen was used. A dozen NeuGuide™ devices designated for this procedure were labeled from 1 to 12. The porcine pelvic ligaments were exposed for a length of at least 15 cm. Using the NeuGuide™ delivery system, the test devices were inserted into the ligament at least 1 cm apart. The pull-out forces were measured in Newtons (N). A force gauge was attached to the suture in the anchor's distal end. The force gauge was set to measure force at peak. Then a tensile force was applied upon the anchor until it pulled out of the ligament. The procedure was performed using all 12 devices. The calculated 95 % lower tolerance interval for the pull-out force of the NeuGuide™ anchors (N) was set to be at least 20 N.

In the second stage of the study we evaluated the functional performance of the device. We performed the test in three different animal laboratories, using three animals, and the device was used by three surgeons who specialize in pelvic floor surgery. Once anesthetized, the pigs were placed in the supine position prepared and draped for surgery as appropriate. The first animal model included the use of 12 anchors (6 on the right and 6 on the left pelvic ligaments). In the second test animal an additional 10 anchors were used, and 20 more anchors were deployed in the third test animal. The animals were monitored for blood pressure and vital signs before and after the procedure. After labeling all the articles, porcine pelvic ligaments were exposed for a length of at least 15 cm. The NeuGuide™ anchor was inserted into the ligament following the instruction guidelines.

The study protocol was reviewed and approved by the Animal Care and Use Committee and was carried out under Good Laboratory Practice conditions.

Cadaver study

The study included three fresh female cadavers with no previous history of pelvic surgery and intact pelvic genitalia. One surgeon who specializes in female pelvic floor surgery performed the procedures. The cadavers were thawed for 72 h before the study. They were placed in the lithotomy position with the pelvis overhanging the operative table. Both SSL were identified transvaginally by palpation using the thimble. When the SSL was identified the needle was inserted through the tunnel on the thimble unit, penetrated the vaginal wall, and was carefully guided to the SSL. When in place, the ligament was penetrated by the needle and the anchor was released and fastened to it. The needle was then retracted back out through the vaginal wall together with the suture that is attached to the anchor. A total of 14 anchors were deployed to the SSL of the cadavers. The pull-out force was measured using the gauge device on two cadavers using 3 anchors on each side (a total of 12 anchors). Thereafter, a laparotomy was performed to demonstrate the position and distance of the anchors and sutures, and to evaluate for potential injury to adjacent tissues or organs. Bladder and rectal wall integrity were evaluated and the distances from the pudendal nerves and vessels were reported. Figure 3

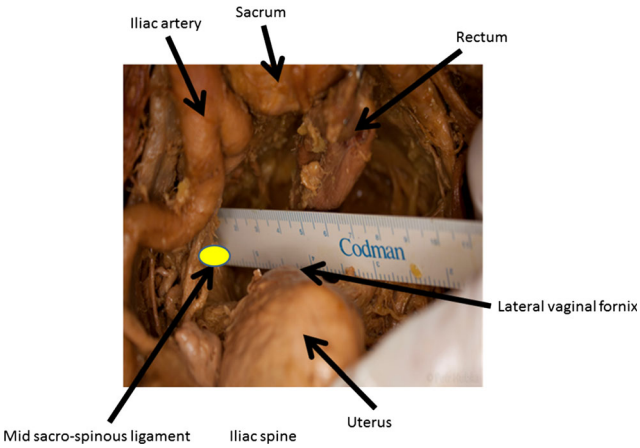

Fig. 3 The anatomical position of the NeuGuide™ anchor in relation to neighboring tissues and structures. The NeuGuide™ anchor is positioned in the mid-portion of the sacro-spinous ligament (*yellow* ellipse); the *arrows* point at the neighboring structures

depicts the anatomical position of the NeuGuide™ anchor in relation to neighboring tissues and structures.

Statistical analysis

To evaluate the mean and calculate the 95 % confidence interval for continuous parameters, while maintaining a type I error of 5 % (=α) and at least 80 % power (=1-β), the minimal sample size is 10; this number does not include drop outs due to unrelated technical failures (which are normally estimated in 10 to 20 %). Therefore, we chose to perform 12 procedures.

The data on continuous variables with normal distribution were presented as mean±SD and upper and lower 95 % mean± SD, and compared in study groups using Student's *t* test. Continuous variables not normally distributed and ordinal variables were presented as medians with inter-quartile range (IQ range). Two-sided *p* value of <0.05 was considered significant.

Results

In the first stage of this study we evaluated the forces (N) required to pull the NeuGuide™ anchor elements from a uniform porcine ligament. All 12 NeuGuide™ anchors were successfully inserted into the porcine ligament 1 cm apart. The pull-out force data from the porcine model are presented in Table 1. The mean pull-out force was 34.13±4.32. None of the measured forces were below 20 N, which was the predefined lower 95 % tolerance interval for the pull-out force of the NeuGuide™ anchors.

In the second stage of our study we evaluated the pull-out forces from a human pelvic floor ligament. Two cadavers were used for this test. Twelve NeuGuide™ anchors were successfully inserted into the SSL (3 on each side of the two cadavers). The pull-out force data from the cadavers are

Table 1 Porcine ligament NeuGuide™ anchor pull-out force

Pull-out force	Porcine	Cadaver
1	32.4	21.1
2	35.1	23
3*	40.08	24.2
4	37.08	31
5	32	49.8
6**	41	42.4
7	34.6	42.7
8	33.3	38.2
9***	26.6	45.9
10	37.8	33.9
11	27	39
12**	32.6	36.9
Mean±SD****	34.13±4.32	35.68±9.28
Maximum	41.00	49.8
Minimum	26.60	21.1
Mean upper 95 %	36.99	41.57
Mean lower 95 %	31.26	29.78

N Newton, *SD* standard deviation

*Comparison between left and right pull-out forces in cadaver 1 p=0.08

**Comparison between pull-out forces in cadaver 1 vs cadaver 2 p=0.19

***Comparison between left and right pull-out forces in cadaver 2 p=0.12

****Comparison between porcine and cadaveric pull-out forces p=0.60

presented in Table 1. The mean pull-out force was 35.68± 9.28. None of the measured forces was below 20 N, which was the predefined lower 95 % tolerance interval for the pull-out force of the NeuGuide™ anchors. No statistically significant difference was noted between the pull-out forces in the porcine and the cadavers (p=0.60). A comparison was made between the mean pull-out forces of the two cadavers and no statistically significant difference was found (p=0.19). A comparison was also made between the pull-out forces on the right and left SSL to evaluate whether the change in position or angle of insertion affects the strength of the holding of the ligament by the anchor. Likewise, no statistically significant difference was found between the sides in the two cadavers (p=0.08 and p=0.12 respectively).

When evaluating the functional performance of the device, no abnormalities or malfunctions were noted. All of the device articles have been verified for conformance. All functional steps were performed successfully.

After performing SSLF on three cadavers, cadaveric laparotomy dissection was performed. On all three cadavers we reached the SSL safely via a transvaginal approach using the NeuGuide™ device guided by the thimble. No damage to the surrounding organs and tissues was demonstrated. We found that in all cases the actual position of the suture in relation to the mid SSL was correct; a safe distance was maintained from

the rectum, bladder, and pudendal nerves and vessels; and the distance from the vagina or uterine cervix to the mid SSL was shortened in all cases.

In two cadavers, the vaginal loose end of the suture was mounted on a virgin needle and passed through the original vaginal entry point, beneath the vaginal wall mucosa, and then it was sutured to the uterine isthmus through a 1-cm high posterior colpotomy. This was rather technically easy to perform, and safe as well, as the needle passage is adherent to the vaginal wall to minimize any possible hazard to the neighboring viscera or blood vessels. At the end of the procedure, we found the uterus to be effectively supported in its proper pelvic anatomical position.

Discussion

Failure of adequate anchor fixation may lead to early dislocation of the devices used for incontinence and prolapse surgery. Most newly developed devices rely on a stable intracorporeal fixation, particularly during the procedure and in the early postoperative phase [18]. Several anchoring systems have been developed including absorbable patches (TVT Secure), anchoring systems with a self-adherent surface (DynaMesh SIS minor) or tapes with minimized anchors such as the MiniArc. Anding et al. [18] claimed that to date, reliable methods of evaluating different types of anchoring systems are lacking and reported an in vitro testing method of different anchoring systems (PelFix, Surelift, TFS, and MiniArc). They found that the systems evaluated showed significantly different pull-out forces. Mechanical strain resulted in deformation, with local peak stresses depending on the mesh structure, size, and form of the anchoring system. Furthermore, they showed that under the condition of form stability, relative differences in pull-out forces did not change in different tissues [18].

In the current study, the test procedure indicated that the NeuGuide™ system is safe for use, as all steps of the procedure have been conducted successfully and all anchors have been deployed and fixed to the desired location upon the porcine and cadaveric ligaments.

Early dislocation of mesh material, sutures or anchors is a major risk factor for failure, especially when miniaturized meshes, slings, and sutures are used. Some of these procedures depend on reliable intracorporeal fixation with an anchoring system that prevents dislocation. Brennand et al. [16] described the initial placement of the Elevate single-incision mesh kit device tips relative to the sacro-spinous ligament, and measured the tip movement over a 6-month period after its initial placement. They found that single-incision mesh kits do not reliably anchor into the sacro-spinous ligament. The tips have been shown to move over time, although not all cases of anchor movement were associated with recurrent prolapse [16].

Since the success of mesh or sling procedures relies on some degree of tension, mechanically reliable anchoring systems are essential. Petros and Ulmsten's integral theory [19] emphasizes the role of the connective tissue of the pelvic floor muscles and the supporting ligaments in both function and dysfunction, and in surgical repair [19]. This led to the defect-oriented concept for repairing pathological conditions of the pelvic floor. The concept of the "tension fixation system" comprises the use of slings to substitute the impaired ligaments, which are usually inserted under direct vision using polypropylene anchors [20]. In our novel device, the NeuGuide™, the anchor unit is designed as a sharp needle-point element, enabling piercing through the selected location on the ligament without the need for vaginal dissection. When released by the applicator it is deployed and thus fixed in place. The anchor incorporates a surgical suture at its distal end, which, following its deployment, enables fixation and the continuation of the surgical procedure.

The degree of tension and stress that pelvic structures bear in daily life, during surgery, and during the early postoperative period (coughing, sitting up) is not precisely known [18]. It is not possible to measure in real life; therefore, necessitating the use of adequate test models. The use of both porcine animal models and cadavers have been previously used and are established as accepted models for the measurement of tensile, tearing, and pull-out forces of meshes, sutures, and anchoring systems [18, 21, 22]. Nevertheless, it should be noted that both types of models are not ideal. The rapid postmortem changes of physicochemical properties of the tissue need to be considered in cadaveric testing. Regarding animal models, although the tissue features of the pig are most easily comparable with those of the humans, this is not so for the pelvic floor. The porcine connective tissue is not as strong as in humans, and some of the basic structures such as the arcus tendineus and the sacro-uterine ligaments seem to be missing in tetrapod vertebrates [17].

Cosson et al. [22] have measured the strength of pelvic ligaments in cadaveric specimens. They found great variability in the values obtained at tearing, with minimal values at around 20 N. They also reported that ligament strength varied between individuals, and in the same patient regarding the type of ligaments and the side involved [22]. In our study, in both the porcine model and in the human cadavers, the pull-out force was greater than 20 N (34.13±4.32 and 35.68±9.28 respectively). Moreover, even the mean lower 95 % (31.26 and 29.78) was greater than 20 N, ensuring that the NeuGuide™ anchors withstand greater pull-out forces. To account for the possible variability between specimens and between sides, we not only compared porcine and cadaveric pull-out forces, but also pull-out forces in cadaver 1 vs cadaver 2, and between the left and right side in both cadavers. None of these comparisons was statistically significant.

It could be claimed that our test results might not be applicable to live patients. Nevertheless, the use of different

animals, multiple deployments of the anchors according to our sample size calculation, and the fact that the procedure was performed by different surgeons, strengthen our encouraging results. We hope to soon start treating live patients who need SSLF using the NeuGuide™ device.

We proved that it is possible to pass the suture, anchored to the SSL, through the original vaginal entry point, beneath the vaginal wall mucosa, and before suturing to the uterine isthmus through a 1-cm high posterior colpotomy. This was technically easy to perform, and safe, because the needle passage is adherent to the vaginal wall to minimize any possible hazard to the neighboring viscera or blood vessels. At the end of the procedure, we found the uterus to be effectively supported in its proper anatomical position in the pelvis.

In conclusion, the new anchoring device we have developed (NeuGuide™) permits the surgeon to perform minimally invasive centro-apical pelvic suspension with no mesh and no deep pelvic dissection. It is aimed at facilitating a durable, easy, and short procedure for SSLF with hypothetically fewer operative complications.

Compliance with ethical standards

Conflicts of interest The author MN is the founder of POP Medical Solutions. All the other authors declare that they have no conflicts of interest.

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