Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

Research Protocol

4 April 2016

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Research Protocol

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Research Protocol

Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

GENERAL INFORMATION

Title: Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

Short Title: How well does the low stretch tension free tape (DynaMesh®-SIS soft) treat stress urinary incontinence in women.

Study Design: Prospective multicentre international observational cohort study.

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Research Protocol

Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

R&D Reference: 2015O&G01M

Clinical Trials Reference: NCT02407145

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Research Protocol

Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

SUMMARY

This study is designed to evaluate the safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension-free midurethral slings in the treatment of stress urinary incontinence (SUI) in women. The efficacy and safety will be reported over two years of follow up.

Stress urinary incontinence is a common problem, affecting large numbers of women. If conservative measures are ineffective then surgery is offered. Surgery involves a permanent mesh sling being placed, tension free beneath the midurethra. The standard retropubic tension-free vaginal tape (TVT) is made of polypropylene. The use of permanent mesh in gynaecology has come under scrutiny in recent years due to significant complications for women.

The sling being studied is DynaMesh®SIS soft, made of polyvinylidene fluoride (PVDF) which has improved biocompatibility with tissues compared to polypropylene. The technique of retropubic placement of the DynaMesh®SIS soft does not differ from current retropubic TVT placement.

The results of the efficacy and safety of DynaMesh®SIS soft will be compared with the safety and efficacy of traditional polypropylene slings, as reported in current literature. It is hypothesised that this sling is non-inferior compared to traditional polypropylene slings in both parameters.

There are eleven research centres in two countries, The United Kingdom and Germany. The DynaMesh®SIS soft sling is currently in use in four of the research hospitals, Norwich (main research centre), Belfast and Antrim in the UK and in Munich in Germany. It will be introduced in London, Cambridge, Upton, Solihull, Huntingdon and Kilmarnock in the UK and Würzburg in Germany..

Women with SUI who are suitable for a retropubic tape and have never had an incontinence operation will be included. They will have urodynamics prior to demonstrate SUI. Participants would complete standardised urinary incontinence and quality of life questionnaires prior to their procedure and at 3,6,12, 18 and 24 months by post. Clinical follow up will occur at 3 and 12 months post operatively and as required if any concerns.

BACKGROUND

Retropubic midurethral slings are a well-established surgical procedure for treatment of stress urinary incontinence in women. The TVT (Tension Free Tape) procedure was introduced by Ulmsten in 1996[1] and has become a standard surgical procedure for stress urinary incontinence. Polypropylene is the traditional mesh used for the procedure. The objective success rate of the retropubic TVT procedure is reported as 80% at 12 months[2], with other longer-term results reported as 85% at 5 years[3] and 90% at 17 years[4].

Recognised complications of the retropubic TVT procedure[5] include postoperative voiding difficulties, new urinary urgency or frequency, bladder injury (0.7% to 24%), bowel injury (<1%), haemorrhage (0.7% to 8%) with 2.8% requiring transfusion and wound infection rate of <1%. The rate of vaginal erosion ranges from 0% to 1.6% and urethral injury or erosion 0.3%.

The safety of mesh implants in gynaecology has been questioned in recent years with a warning issued by the FDA[6] in 2011. The Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK released its conclusions regarding mesh use in gynaecology in October this year. After review of available information the MHRA has stated that the benefits of vaginal mesh implants outweigh the risks and there is no remove these devices from practice in the UK. Regarding safety there was no evidence that one device differed from another. Ongoing review of information about mesh use will continue and would consider post-market clinical follow-up as important in terms of monitoring usage and safety.[7]

The suitability of mesh for implantation depends on the following qualities of the mesh – biocompatibility, stability, effective porosity and elasticity. The surgical expertise and patient selection are also generally recognized as factors in safe use of vaginal mesh.

The following ideal properties have been proposed for pubovaginal slings – large pore size (>1mm) mesh with minimal elasticity, width of 10mm with no change in width under tension, blunt edges and made of a permanent material with limited tissue reaction – with little resulting fibrosis and shrinkage[8].

Polyvinylidene fluoride (PVDF) monofilament thread has high stability over time, its surface does not degrade and the thread does not become brittle or lose significant tensile strength over time, both in vitro and in vivo in animal experiments[9,10]. PVDF is used as a suture material in cardiovascular surgery. The material was investigated as an alternative material for mesh implants for abdominal hernia repair in 2002 in an animal model[11]. As an implant material PVDF continued to have high biocompatibility with reduced fibrosis and scar formation compared with convention implant materials made of polypropylene[12]. PVDF mesh has been shown to be a suitable material for

the use in abdominal hernia surgery with high success rates and low rates of infection and bowel adhesion[13,14].

PVDF slings have been in use since 2006, marketed as DynaMesh®-SIS. The design of the sling was modified in 2011 by reducing the diameter of the individual PVDF threads to create DynaMesh®-SIS soft. DynaMesh®-SIS soft is warp knitted from polyvinylidene fluoride (PVDF) thread and measures 1cm wide and 50cm long. It is specifically designed for its use as a midurethral sling for the treatment of female stress urinary incontinence. The mesh is macroporous and has low elasticity meaning it maintains its dimensions, and as a result pore size, when under tension. This also means that the load of the sling on the urethra is dissipated over a larger surface area. Compared to conventional polypropylene mesh DynaMesh®-SIS has a reduced reactive surface area with high effective porosity[15]. As each sling is individually knitted it has soft edges and does not require plastic sheath for smooth movement through tissues[8].

The above properties of DynaMesh®-SIS soft make it an attractive alternative to traditional polypropylene slings. The surgical procedure for inserting the DynaMesh®-SIS soft retropubically does not differ from current retropubic TVT placement, therefore the same procedural risks exist. Given its physical properties the exposure and erosion rate of DynaMesh®SIS soft sling are not thought to be greater than that of traditional polypropylene slings.

Research Protocol

Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

HYPOTHESIS

PVDF (DynaMesh®SIS soft) sling is non-inferior to traditional retropubic midurethral slings in the treatment of stress urinary continence, when compared to the reported safety and efficacy of retropubic polypropylene midurethral slings in current literature.

AIM

To investigate the safety and efficacy of the low-elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic midurethral sling in the treatment of stress urinary incontinence in women.

PRIMARY OUTCOME

- The subjective cure rate of retropubic midurethral PVDF slings in treating stress urinary incontinence.
- The rate of complications of retropubic midurethral PVDF slings, in particular mesh erosions.

SECONDARY OUTCOMES

- Changes in quality of life, with regards to urinary symptoms, following placement of a retropubic midurethral PVDF sling.
- The subjective cure rate of retropubic midurethral PVDF slings in treating stress urinary incontinence compared to the reported cure rate for traditional polypropylene retropubic slings.
- The rate of complications of retropubic midurethral PVDF slings, in particular vaginal erosions and how the rates of complications compare to those reported in the literature for traditional polypropylene retropubic slings.

RESEARCH DESIGN AND METHODS

Study design

A prospective multicentre international observational cohort study.

Study centers

Eleven centers in two European countries – nine in the United Kingdom – Norwich, Cambridge, Huntingdon, London, Upton, Solihull, Kilmarnock, Belfast and Antrim and two in Germany – Munich and Würzburg.

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Responsible surgeons

Thirteen responsible surgeons are involved at the eleven study centres, they include three urogynaecologist and ten gynaecologists with a special interest in urogynaecology.

Current practice

DynaMesh®-SIS and DynaMesh®-SIS soft are used routinely used in two of the research centres – Antrim (6 years), Belfast (5 years), Munich (2 years) and Norwich (1.5 years).

Language

All documents will be translated in to German for the centres in Germany, coordinated by the centres in Germany. There are German versions of the study questionnaires already available.

Study Plan

Recruitment

Attends routine outpatient visit – stress incontinence identified

- Routine management commenced
- Deemed appropriate for Multichannel Urodynamics
    - results prove urodynamic stress incontinence

Follow up outpatient visit - identified as being suitable for a midurethral sling

- Check inclusion/exclusion criteria
- Introduce the concept of the study
- Give Consent for Contact letter and inform local researcher
- If immediately interested in study give Participant Information Sheet and inform local researcher

1) Consent visit

- Surgical consent taken by surgeon or their team
- Obtain written consent for surgical procedure – three copies – patient, medical notes and participant file
- Obtain consent for BSUG database (UK participants)
- Research consent obtained by local researcher or assistant
- Obtain written consent for study – three copies – patient, medical notes and participant file
- Assign study number – record in data collection form
- Complete baseline data
- Record urodynamic results
- Ask to complete preoperative questionnaires and calculate scores by adding item scores
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
    - Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Send participation letter to GP
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

2) Day of surgery

- Attend research centre for procedure
- Document surgical parameters
- Document surgical complications and outcomes
- Document success of trial of voids

3) Clinical Review – three months post operatively

- Document if dry from stress urinary incontinence
- Document if experience urinary urgency
- Document if experiencing any difficulties in voiding
- Document if experiencing pain at site of tape
- Document if experiencing vaginal discharge
    - Perform vaginal examination
    - Document mesh erosion – presence, size and site
    - If present inform responsible surgeon or their medical staff for management plan
- Ask to complete study questionnaires and calculate scores by adding item scores
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
    - Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Forward operative and three month follow up data to Research Fellow at Norwich Research Centre
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

4) Six months post operatively

- Send out study questionnaires with reply paid envelopes
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
- Contact participant if not received back after 4 weeks
- Calculate scores by adding item scores
- Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Collate responses in participant file
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

5) Clinical Review – twelve months post operatively

- Document if dry from stress urinary incontinence
- Document if experience urinary urgency
- Document if experiencing any difficulties in voiding
- Document if experiencing pain at site of tape
- Document if experiencing vaginal discharge
- Document if sexually active, if yes if any problems
    - Perform vaginal examination
    - Document mesh erosion - presence, size and site
    - If present inform responsible surgeon or their medical staff for management plan

- Ask to complete study questionnaires and calculate scores by adding item scores
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
    - Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Forward six month and twelve month data to Research Fellow at Norwich Research Centre
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

6) Eighteen months post operatively

- Send out study questionnaires with reply paid envelopes
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
- Contact participant if not received back after 4 weeks
- Calculate scores by adding item scores
- Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Collate responses in participant file
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

7) Twenty-four months post operatively

- Send out study questionnaires with reply paid envelopes
    - ICIQ-FLUTS
    - ICIQ-LUTSqol
- Contact participant if not received back after 4 weeks
- Calculate scores by adding item scores
- Record individual answers for ICIQ-FLUTS questions 9a, 11a, 12a
- Collate responses in participant file
- Forward eighteen month and twenty-four month data to Research Fellow at Norwich Research Centre
- If depression is identified on ICIQ-LUTSqol (Question 12) inform participant GP for further follow up

Study completion

- Send letter thanking participants for their involvement and communicating results

Study Population

Eligibility

Eligible participants will be identified from routine referrals to the outpatient gynaecology and urology clinics of the responsible surgeons. Those women who present with symptomatic stress urinary incontinence and subsequently have proven urodynamic stress incontinence may be eligible for enrollment in the study.

Participant inclusion criteria

- Women with proven urodynamic stress incontinence deemed suitable for retropubic midurethral sling procedure as per the treating surgeon.
- Only women having sling placement as their primary incontinence procedure without any concomitant prolapse procedure will be included.

Participant exclusion criteria

- Urodynamic studies negative or inconclusive for stress urinary incontinence.
- Previous incontinence surgery or planned concomitant prolapse surgery.
- Not speaking English or German, depending on study centre.
- Lacking the capacity to consent.

Recruitment

Following urodynamic studies and confirmation that a midurethral sling is appropriate, as the next step in management of their stress urinary incontinence, they will be offered a midurethral sling. If they meet the eligibility criteria a member of the site research team with explain the study, give them time to ask questions and give them the Participant Information Leaflet. The potential participants will be informed that participation in the study in voluntary. Potential participants will have at least 24 hours to consider their participation in the study. They will have until their surgical consent visit to consider their participation, in clinic practice this may be several weeks.

Withdrawal of consent

Participants may withdraw from the study at any time. Any data already collected with still be used, however no further questionnaires will be sent and no 12 month follow up will occur. If participants withdraw consent on the day of surgery they may still have their procedure but no study data will be collected. If consent is withdrawn prior to their three month follow up they will require follow up but no study data will be collected.

Study Procedures

Pre-enrollment investigation

Multichannel conventional urodynamics proving urodynamic stress incontinence must be performed to confirm eligibility for inclusion in the study

Consent visit

A consent visit will occur prior to the day of surgery. At this visit consent will be obtained for both the surgical procedure and participation in the study.

Surgical consent will be obtained by the surgeon or their team. For participants in the UK they will also be asked to consent to collection of operative data on the British Society of Urogynaecologists (BSUG) database. Surgeons who are members of BSUG are encouraged to enter their surgical cases on the BSUG database for ongoing personal, local and national audit of surgical procedures, their outcomes and complications for all urogynaecology procedures.

Research consent will be obtained by a member of the site research team. They will again explain the study to the participant and ensure their study related questions are answered. The participants will be informed that their participation is voluntary and that they may withdraw their consent at any time without any impact on their care.

Participants will be asked to complete the ICIQ_FLUTS and ICIQ-LUTSqol questionnaires prior to their surgery. If depression is identified on the ICIQ-LUTSqol questionnaire (question 12) the researcher will contact the participant's primary care doctor for follow up.

Operative procedure

- The surgery will be performed by either the responsible surgeon, a competent surgeon at the site as agreed by the responsible surgeon or a supervised trainee.
- All procedures to be included in the study will be performed via the retropubic approach, either "bottom-up" or "top-down", with check cystoscopy after sling placement.
- Tensioning of the sling to be performed using the Hager 8/4 technique – Hager size 8 cervical dilator placed in urethra and size 4 between the sling and urethra for standardisation of tensioning and maintaining the same distance between urethra and the tape.
- The choice of anaesthesia and dissection technique (hydrodissection etc.) will be left to individual surgeon.
- Operative antibiotic prophylaxis as per local protocols.
- Post-operative trial of voids as per local protocols.

Clinical follow up visits

- Clinical follow up will be undertaken at 3 months and 12 months by the surgeon, their medical staff, specialist nurse or research nurse.
- This will include subjective evaluation of patient symptoms – dryness from stress urinary incontinence, pain, urgency, normal voiding and whether they are sexually active, and if so if there are any concerns.
- A vaginal examination will be performed to document the presence of mesh erosion and its size and location if present. Management of the erosion will be planned as per the local surgical team and recorded.
- Further investigation or treatment of residual urinary symptoms will also be documented.
- The two validated questionnaires will be repeated.
- If depression is identified on the ICIQ-LUTSqol questionnaire (question 12) the researcher will contact the participant's primary care doctor for follow up.
- Travel costs for the twelve month follow up visit will be reimbursed by arrangements made by each research centre.

Questionnaire follow up

- The two study questionnaires will be posted to study participants at intervals 6, 18 and 24 months post operatively.
- If they have not been returned within 4 weeks the participants will be contacted by their research centre.
- Reply paid envelopes for return of the questionnaires will be arranged by each research centre.
- If depression is identified on the ICIQ-LUTSqol questionnaire (question 12) the researcher will contact the participant's primary care doctor for follow up.

Data Collection

Patient Questionnaire Data

All questionnaires are available in both English and German.
Completed preoperatively, 3, 6, 12, 18 and 24 months postoperatively.

Validated incontinence questionnaires – International Consultation on Incontinence Modular Questionnaire (ICIQ)

- ICIQ-FLUTS
  - 13 questions including date of birth
  - Takes 5 minutes to complete
  - Three scores obtained:
    - F score – scored 0-15 by adding item scores 2a-5a to assess bladder filling symptoms
    - V score – scored 0-12 by adding item scores 6a-8a to assess voiding function
    - I score – scored 0-20 by adding item scores 9a-13a to assess incontinence
    - Individual questions assess presence of:
      - Urge incontinence (9a)
      - Stress incontinence (11a)
      - Other incontinence (12a)

Validated urinary quality of life questionnaire

- ICIQ-LUTSqol
  - 22 questions including date of birth and gender
  - Takes 10 to 15 minutes to complete
  - Scored 19-76 (by adding item scores) with increased score indicating more significant impact on quality of life

Preoperative data

- Demographics
  - age
  - BMI
- Obstetric and gynaecology history
  - Parity
  - pelvic floor exercises
  - previous prolapse surgery
- Multichannel conventional urodynamics
  - presence of urodynamic stress incontinence (inclusion criteria)
  - uroflowmetry – Q_{max} (mL/sec)
  - residual volume
  - presence of detrusor overactivity
  - pressure flow study $P_{detQmax}$ (cmH20)

Operative data

- Intraoperative POP-Q findings
- Method of anaesthesia
  - retropubic infiltration
  - general anaesthesia, sedation
- Surgical approach
  - "bottom-up"
  - "top-down"
- Intraoperative complications
  - bladder injury
  - urethral injury
  - bowel injury
  - estimated blood loss
  - retropubic hematoma
  - vaginal hematoma
  - return to theatre
  - significant pain (admission required)
- Postoperative voiding
  - successful trial of void
  - discharge home with catheter
  - postoperative day of successful trial without catheter

Clinical follow up data – 3 month and 12 month

- Presence of
  - Stress urinary incontinence
  - urinary urgency
  - difficulties in voiding
  - pain at site of tape
  - vaginal discharge
  - sexual activity and presence of problems
- Presence of mesh erosion
  - site – central or in lateral sulci
  - size of erosion
  - management plan
- Study questionnaire scores
  - ICIQ-FLUTS
  - ICIQ-LUTSqol
- Ongoing management
  - Topical estrogen
  - Surgery
  - Suturing
  - Excision exposed mesh
  - Removal of sling
  - Anticholinergic
  - Urodynamic Studies

Research Protocol

Safety and efficacy of low elasticity polyvinylidene fluoride (DynaMesh®-SIS soft) retropubic tension free midurethral sling in the treatment of stress urinary incontinence in women.

Investigational Medical Device

DynaMesh®-SIS soft

Physical properties
DynaMesh®-SIS soft is warp knitted from polyvinylidene fluoride (PVDF) thread and measures 1cm wide and 50cm long.

Intended purpose
Midurethral sling for surgical treatment of stress or mixed urinary incontinence.

Manufacturer
FEG Textiltechnik Forschungs- und Entwicklungsgesellschaft mbH
Prager Ring 70
Aachen
52070
GERMANY

Safety

Adverse Events

The procedure for placement of a retropubic midurethral sling is well established. There are recognised complications. Those complications related to the procedure are:

- bladder perforation
- haemorrhage and retropubic hematoma
- difficulty with bladder emptying
- infection – wound and urinary
- pain
- mesh erosion into the vagina and urethra
- bowel injury (rare).

The procedure for introducing DynaMesh®-SIS soft slings retropubically does not differ from the established procedure for inserting traditional retropubic polypropylene slings, therefore the complications are not expected to differ.

For adverse events that are not considered serious they should be recorded in the participant file as part of the research data in monitoring the safety of the PVDF sling. The Principal Investigator will report to the Sponsor if adverse events are occurring at a greater than expected frequency.

Definition of Serious Adverse Events

The definition of a Serious Adverse Event (SAE) is any adverse occurrence that:

- results in death
- is life-threatening
- requires hospitalisation, or prolongation of existing inpatients' hospitalisation.
- results in persistent or significant disability or incapacity
- is otherwise considered medically significant by the investigator
- is a congenital anomaly or birth defect

Reporting of Serious Adverse Events

If a complication is deemed to be a SAE the Principal Investigator they will report to the Chief Investigator and Sponsor as soon as possible after becoming aware of the SAE and within 24 hours for further assessment by the Sponsor as per NNUH SOP 206 for adverse events. This will be done by way of completion of a SAE form sent directly to the Chief Investigator and Sponsor.

Follow up of Adverse Events

Each research centre has procedures in place for management of complications. Complications occurring for individual participants will be

managed as per local procedures, recorded in participants medical and research file and notified to the main research centre as part of data reporting.

If a participant attends hospital for emergency review thought to be related to their retropubic sling the research team will be informed and documentation of the event added to the participant file.

Complications are reported routinely by way of the BSUG database in the UK.

ANALYTICAL METHODS

Number of study participants

Comparing a success rate of 85% for DynaMesh®-SIS soft versus 80% cure at one year for the polypropylene retropubic tapes, as reported in literature, with a non-inferiority margin of 2% a power of 80% and type I error rate of 5%, a sample size of 197 is required to detect a difference greater than the non-inferiority margin, given such a difference does exist.

Allowing for a 10% drop of rate a total sample size of 218 will be recruited.

Data Analysis

Efficacy

The rate of cure at 3,6,12,18 and 24 months with 95% confidence intervals will be reported.

Cure will be defined as:

- The rate of reported “dryness” from stress urinary incontinence at three and 12 months with 95% confidence intervals.
- Scoring of the ICIQ-FLUTS question 11a score – a score of 0 to 1 representing no or minimal symptoms representing cure. The rate of cure reported as percentage with 95% confidence intervals.

Subgroup analysis

- Evaluation of efficacy with exclusion of the "top-down" cases.

Improvement in incontinence symptoms

- Change in questionnaire scores for urinary incontinence (ICIQ-FLUTS I score)
- To calculate whether or not there has been a significant improvement between pre and post-operative questionnaire scores a Wilcoxon sign rank test will be applied to each questionnaire at each study point (3,6,12,18,24 months).

Efficacy in comparison with polypropylene slings:

The PVDF sling can be assumed to be as effective as traditional polypropylene midurethral retropubic slings if the confidence interval includes 78%, with a non-inferiority margin of 2% compared with reported efficacy of 80% at 12 months for polypropylene midurethral retropubic slings.

Occurrence of de novo urinary symptoms

- Urgency/filling symptoms – ICIQ-FLUTS F score
- Voiding symptoms – ICIQ-FLUTS V score
- Urge incontinence – ICIQ-FLUTS question 9a
- Other incontinence – ICIQ-FLUTS question 12 a

- To calculate whether or not there has been a significant increase (ie worsening of symptoms) between pre and post-operative questionnaire scores a Wilcoxon sign rank test will be applied to each of the above questionnaire scores at each study point (3,6,12,18,24 months).

Safety

- The rates of complications will be presented as percentages with 95% confidence intervals and reported in relation to complication rates reported in current literature related to the traditional TVT.
- Complications reported will be intraoperative complications – bladder injury, urethral injury, bowel injury, estimated blood loss
- Postoperative complications – retropubic hematoma, return to theatre, voiding difficulties

Quality of life:

- Change in quality of life scores -ICIQ-LUTSqol
- To calculate whether or not there has been a significant improvement between pre and post-operative questionnaire scores a Wilcoxon sign rank test will be applied to each questionnaire at each study point (3,6,12,18,24 months).

Interim analysis

- Interim analysis will be performed after 12 months to assess for safety of the procedure
- This will evaluate the rates of recognised complications occurring perioperatively and at the three month follow up.

Data Handling

Source Data

All participants will be assigned a unique study number based on their research centre and recruitment number. Personal data (name, address, date of birth and hospital number) for each participant will be kept locally only and not shared outside the local research team.

Research data will be collected locally via data collection sheets and be identified by unique study number only. These will be scanned and emailed to the named Research Fellow at Norfolk and Norwich University Hospital for entry into the research database at three intervals – after the 3 month follow up, after the 12 month follow up and at 24 months. The Research Fellow will confirm receipt of each data collection sheet and collate on the central study database.

Data from Germany will be collated electronically by a study representative and sent to the Research Fellow at the main research centre at 3 months, 12 months and 24 months.

Unique study numbers

These will be allocated at the time of the consent visit. The numbers will reflect the country, research centre and participant number at the site reflecting sequential recruitment.

Codes

Country		Centre	
United Kingdom	UK	Norwich Cambridge London Huntingdon Upton Solihull Kilmarnock Belfast Antrim	01 02 03 04 05 06 07 08 09
Germany	DE	Munich Würzburg	10 11

Hence the first participant recruited to Munich, Germany will have the unique study number DE-10-01

Individual centres will be responsible for ensuring continuity of unique study number throughout the study.

Data Protection

Personal data will be required for sending out study questionnaires and for arranging follow up appointments, this database will be stored on password protected NHS computers within the United Kingdom.

Research data will be transferred electronically as an email attachment from study centers to the principal study center, participants will be identifiable by unique study number only.

Data collected during the course of the research will be kept strictly confidential and accessed only by members of the trial team. Participant's details will be stored on a secure database under the guidelines of the 1998 Data Protection Act and regular checks and monitoring are in place to ensure compliance. Data are stored securely in accordance with the Act and archived to a secure data storage facility. The senior IT manager (in collaboration with the Chief Investigator) will manage access rights to the data set.

Participants' details will be anonymised on the secure database. To comply with the 5th Principle of the Data Protection Act 1998, personal data will not be kept for longer than is required for the purpose for which it has been acquired.

STUDY ADMINISTRATION

Funding

Kebomed UK, Distributor of medical devices and surgical implants.
Unit 7 Kingsford Rural Business Centre
Kentisbeare
Cullompton
Devon
UNITED KINGDOM
EX15 2AU

Ethical Issues

Approval to be sought by the research committees.
United Kingdom: NRES Committee East of England - Cambridge South
Germany
No recruitment will occur until ethics approval has been granted.

Risks and burdens to participants

- Procedural
  - There are no physical risks to participants associated with the insertion of a retropubic DynaMesh®-SIS soft above those associated with insertion of the traditional polypropylene retropubic midurethral sling. The surgical procedure will not be altered from normal clinical practice.
  - The risk to participants of mesh exposure or erosion is unknown. The researchers believe that because of the physical properties of PVDF and DynaMesh®-SIS soft, as previously outlined, the risk is not likely to be greater than that associated with traditional slings
- Time
  - Time to complete questionnaires – this has been considered and the number of questionnaires minimised
- Financial
  - Financial costs to participants will be limited by supplying reply paid envelopes for return of research questionnaires and reimbursement of travel costs for the 12 month follow up, which is additional to routine postoperative care. Arrangements for postage costs and reimbursements will be organised by individual research centres.

Potential benefits to participants

- Ongoing postoperative support**.**

DISSEMINATION OF RESULTS

Safety data and Serious Adverse Events

Safety concerns or new information regarding the PVDF sling (DynaMesh®-SIS soft) will be communicated to the Sponsor by the Principle Investigator .

Participants will be notified by letter of new information regarding the product.

Publication of results

Results of this study will be published as research articles at follow up intervals of 6, 12, 18 and 24 months. The results will also be submitted for presentation at medical conferences.

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APPENDICES

Permission to Contact – Version 1.1 (Attached as separate document)

Participant Information Sheet - Version 1.5(Attached as separate document)

Participant Consent Form - Version 1.2 (Attached as separate document)

Letter to GP - Version 1.2 (Attached as separate document)

Data Collection Form - Version 1.2 (Attached as separate document)

ICIQ-FLUTS (Attached as separate document)

ICIQ-LUTSqol questionnaire (Attached as separate document)