TOPAS™ System: Safety Information

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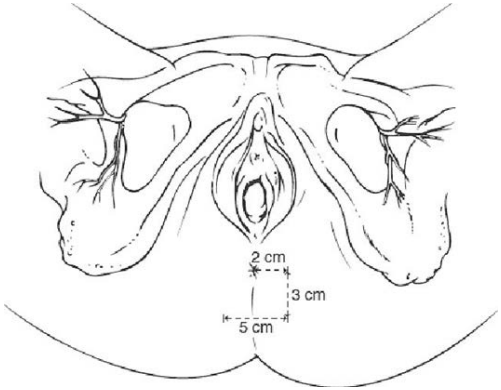
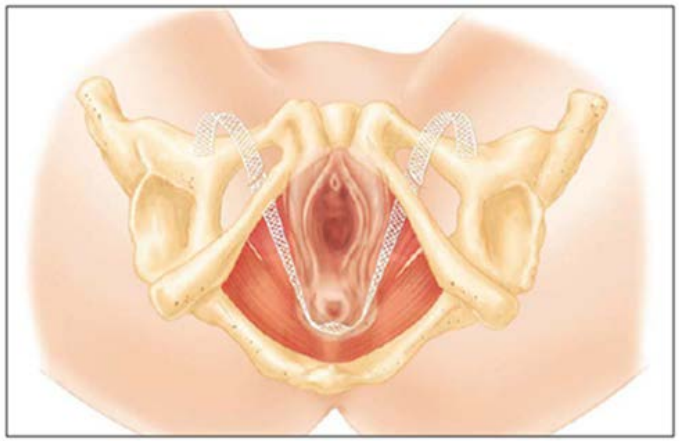
TOPAS Implantation

- Bilateral Perianal Incisions, 2-cm lateral and 3-cm posterior to midpoint of anal verge
- Creation of 2-cm deep subcutaneous tunnel between incisions
- Mesh Drawn into Tunnel
- Bilateral medial thigh 1-cm incisions



TOPAS Implantation

- TOPAS Trocar Placement through Obturator Foramen
- Withdraw Trocar and Mesh Assembly through thigh incision
- “Tensioning” of Mesh



Four Device Malfunctions

- "Gave Way" during tensioning (2)

  Pelvic Area Pain AE (ID # 1009-014-AE01)

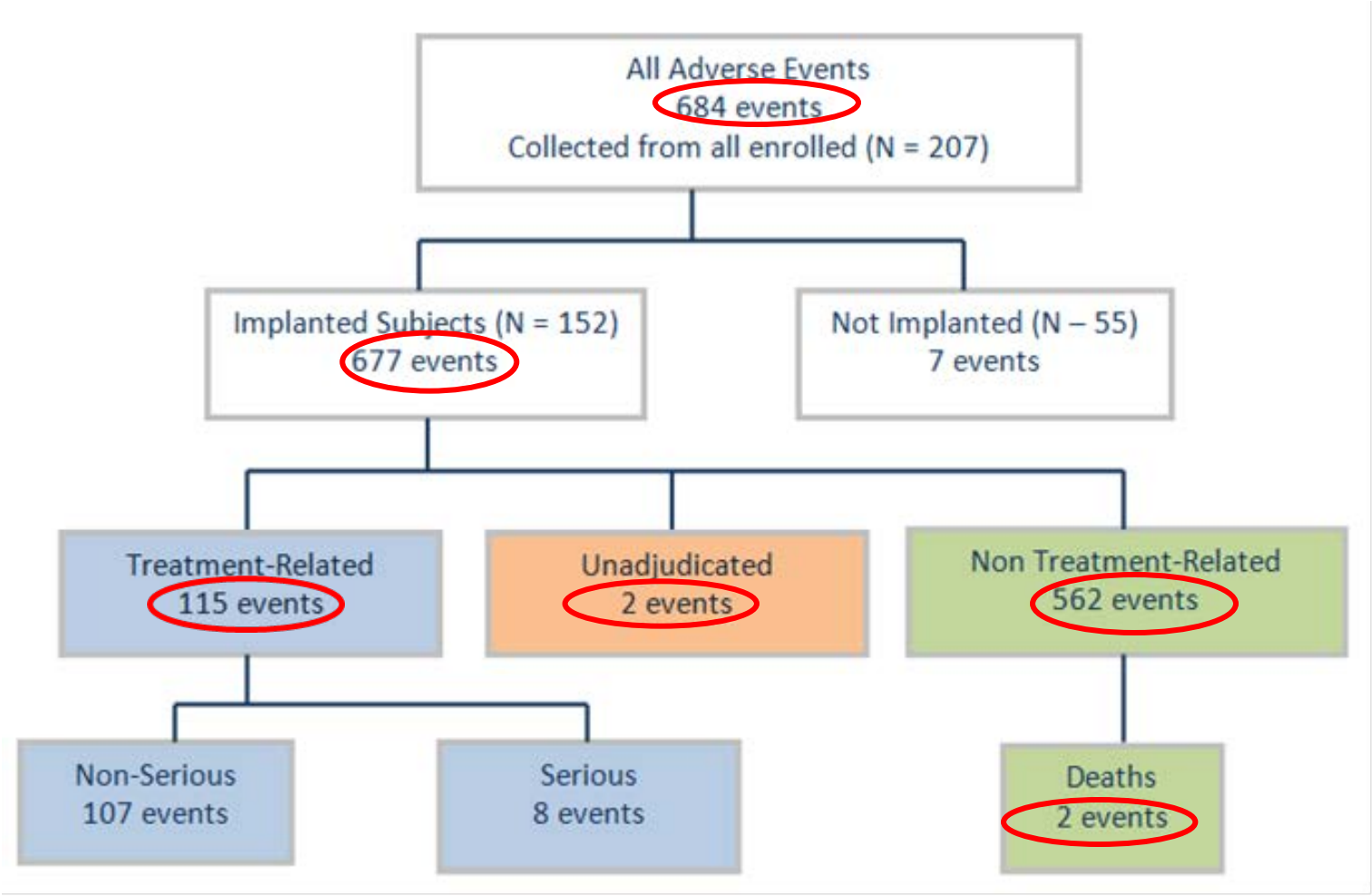
  - "Sitting on sharp rock"
  - Duration: 306/550 days
  - Acupuncture, Narcotic use
- Defective Markings on Mesh (1)
- Mesh Sheath Retraction (1)

Mechanism of Action

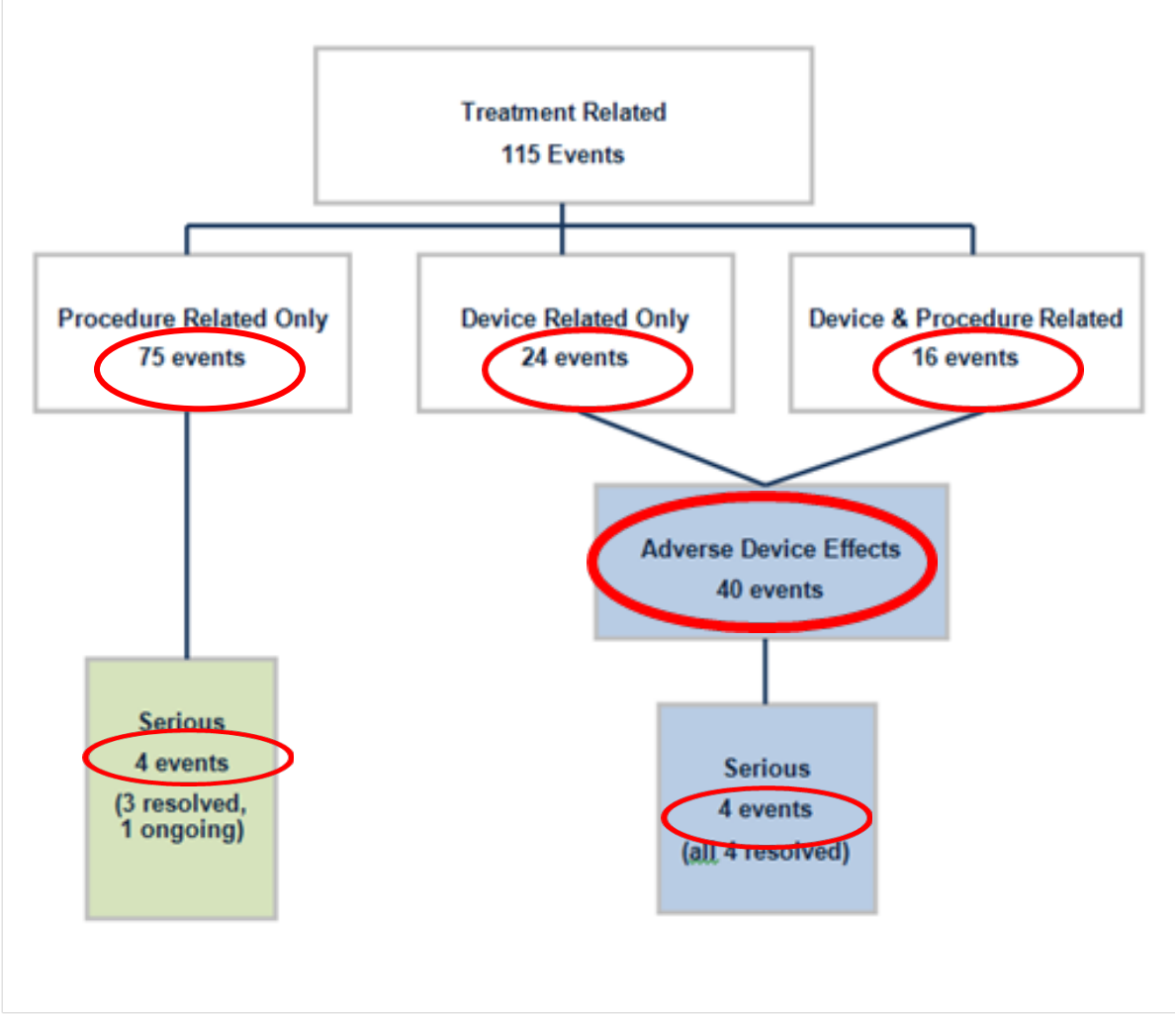
- TOPAS System → Puborectalis Muscle → Supports anorectal angle (ARA)
  - Acute ARA - Retains Stool in rectum at rest
  - Obtuse ARA- Allows passage of Stool by Relaxation of puborectalis muscle

Panel: Discuss Rates of Pelvic Organ Prolapse and Relationship to TOPAS System

All Adverse Events: Overview



Treatment-Related Adverse Events



Treatment-Related Adverse Events: Summary

AE Category	Treatment-Related AEs		Device-Related AEs (ADE)		Unresolved AEs
	N (%) AEs (n=115)	N (%) of Subjects (n= 152)	N (%) AEs (n=40)	N (%) of Subjects (n= 152)	N (%) AEs (n=115)
Pelvic Area Pain	50 (43.5%)	43 (28.3%)	23 (57.5%)	21(13.8%)	9 (7.8%)
Infections	25 (21.7%)	22 (14.5%)	2 (5.0 %)	2(1.3%)	0 (0%)
Pelvic Organ Prolapse	13 (11.3%)	9 (5.9%)	10 (25%	7(4.6%)	7(6.1%)
Urinary Problems[#]	8 (7.0%)	8 (5.3%)	2 (5.0%)	2(1.3%)	3 (2.6%)
Defecatory Problems	4 (3.5%)	4 (2.6%)	0(0%)	0(0%)	2 (1.7%)
Bleeding	1 (0.9%)	1 (0.7%)	0(0%)	0(0%)	0
Other	14 (12.2%)	14 (9.2%)	3(7.5%)	3(2.0%)	1 (0.9%)
TOTAL	**115**	**72(47.4%)**	**40(34.8%)**	**33(21.7%)**	**22 (19.1%)**

Serious Adverse Event: Definition

- Death
- Life-threatening Adverse Experience
- In-patient Hospitalization
- Persistent or Significant Disability
- Congenital Anomaly/ Birth Defect
- Important Medical Event

Not all surgical interventions → SAEs

Four Procedure-Related SAEs

1. Exacerbation of Post-Traumatic Stress Disorder (PTSD)
2. Deep Vein Thrombosis (DVT)
3. Chronic Obstructive Pulmonary Disease (COPD)
4. Methicillin-Resistant Staphylococcus Aureus (MRSA) hand infection

Four Device-Related SAEs

1. Worsening Buttock and/or Sciatic Pain
2. De Novo Pelvic Organ Prolapse (POP)
3. De Novo Pelvic Organ Prolapse (POP)
4. Worsening Pelvic Organ Prolapse (POP)

All Resulted in Surgical Intervention

Five Additional Surgical Interventions:

- Worsening Pelvic Organ Prolapse (2)
- Worsening Rectal Prolapse (POP)
- De Novo Cystocele (POP)
- Worsening Urge Incontinence

Unresolved Adverse Events

- Treatment-related AEs: 19.1% (22/115) unresolved in 21 subjects
  - Pelvic pain (9)
  - Pelvic organ prolapse (7)
  - Urinary incontinence (3)
  - Worsening fecal incontinence (2)
  - Other (1)

Pelvic Area Pain

Pelvic Area Pain: Aggregated

- Pelvic Pain – 13 subjects (8.6%)
- Buttock Pain – 12 (7.9%)
- Groin Pain – 8 (5.3%)
- Leg Pain – 7 (4.6%)
- Urogenital Pain – 5 (3.3%)
- Abdominal Pain – 1 (0.7%)

Pelvic Pain Analysis: Shortcomings

- Numeric Pelvic Pain Scale (NPPS)
  - Frequency: Acute postop, 3, 6,12 month
  - Assessment limited to preceding 24-hrs
  - Limited Data Collection
    - 103/152 Subjects at Baseline
    - 91/152 Subjects at 12 months

Treatment-Related AE: Pelvic Pain

AE Category	Total AEs N	Time to Onset				Duration				Unresolved Pain AEs N(%)
		Mean Days	≤ 30 Days	31-120 Days	121+ Days	Mean Days	≤ 30 Days	31-120 Days	121+ Days	
Pelvic Pain	50	81.9 ± 196.0 (0 - 1004)	34 (68.0%)	8 (16.0%)	8 (16.0%)	313.0 ± 454.9 (0 - 1536)	21 (42.0%)	8 (16.0%)	21 (42.0%)	9 (18.0%)

Pelvic Area Pain: Unresolved

Event ID	Symptoms	Onset Days from Implant	AE Duration	Interventions
1009-016 AE02	Abdominal pain/spasms	148	1297	Bentyl, high fiber
1009-018 AE02	Pelvic Pain	379	1066	None
1009-028 AE02	Right hip pain (Sciatic-like)	99	1076	None
1016-013 AE04	Sharp, intermittent Rectal pain (when sitting)	40	1140	None
1019-004 AE01	Stabbing Rectal pain at times; dull at other times	202	1314	None
1056-006 AE08	Increased Buttock & lower back Pain	0	1536	None
1078-002 AE03	Episodic Perianal Pain & Spasms	36	1264	Valium
1078-005 AE01	Perianal Pain & Lower Vulvar Pain	14	1249	Narcotic Pain meds
1078-001-AE02	Intermittent Tailbone Pain	862	401	None

Pelvic Pain: Assessment

- NPPS Questionnaire
- Annual Q-tip rectal palpation for pain, infection, and erosion
- Digital Rectal exam (DRE) at years 4 & 5

Discussion Points for the Panel:

  - Adequacy of Pelvic Pain Characterization and Evaluation
  - Possible Etiologies of the Pain that might require additional Diagnostic Studies

Pelvic Area Pain: Post-Hoc Analysis

Covariates: Implanter Medical Specialty, Age, BMI, Parity, Baseline PFDI Score, Responder50, Medical Hx

Implanter Medical Specialty:

- Number of Treatment-Related AEs:
  - *Colorectal surgeons: 45.0% (27/60)* ***versus*** *Urogynecologists: 17.4% (16/92) $p < 0.001$*
- Median Time to Onset of Pelvic Area Pain
- Median Duration of Pain
- Pelvic Pain Resolution

Results depend on 2 large urogynecology sites with stretching instructions.

Pelvic Organ Prolapse

Treatment-Related AEs: Pelvic Organ Prolapse

Adverse Event Description	Total Treatment-Related AEs N (%) n= 115	Total Subjects N (%) N=152	SAEs N (%) n= 115	Surgical Treatment N (%)
Pelvic Organ Prolapse	**13 (11.3%)**	**9 (5.9%)**	**3 (2.6%)**	**7 (54%)**
***De Novo* POP:**	**8 (7.0%)**	**7 (4.6%)**	**2**	**3 (23%)**
Rectal Prolapse	2	*	1	1
Rectocele	4	*	0	0
Cystocele	1	*	0	1
Enterocele	1	*	1 (combo)	1
Worsening POP:	**5 (4.3%)**	**3 (2.0 %)**	**1**	**4 (31%)**
Rectal Prolapse	3	*	1	2
Rectocele	1	*	0	1
Enterocele	1	*	0	1

Treatment-Related AEs: Pelvic Organ Prolapse

AE Category	Total AEs N	Time to Onset				Duration				Unresolved N (%)
		Mean Days	≤ 30 Days	31-120 Days	121+ Days	Mean Days	≤ 30 Days	31-120 Days	121+ Days	
Pelvic Organ Prolapse	**13**	**350.9 ± 282.6 (76 - 869)**	**0 (0.0%)**	**1 (7.7%)**	**12 (92.3%)**	**608.0 ± 463.4 (0 - 1259)**	**1 (7.7%)**	**2 (15.4%)**	**10 (76.9%)**	**7 (53.8%)**
De Novo Prolapse	8	442.9 ± 322.6 (128 - 869)	0 (0.0%)	0 (0.0%)	8 (100.0%)	695.6 ± 424.5 (100 - 1259)	0 (0.0%)	1 (12.5%)	7 (87.5%)	5 (62.5%)
Worsening Prolapse	5	203.8 ± 116.3 (76 - 370)	0 (0.0%)	1 (20.0%)	4 (80.0%)	467.8 ± 537.5 (0 - 1075)	1 (20.0%)	1 (20.0%)	3 (60.0%)	2 (40.0%)

Other Treatment-Related Adverse Events

Treatment-Related AEs: Defecatory Problems

AE Category	Total AEs N	Time to Onset				Duration				Unresolved N (%)
		Mean Days	≤ 30 Days	31-120 Days	121+ Days	Mean Days	≤ 30 Days	31-120 Days	121+ Days	
Defecatory Problems	4	103.8 ± 155.7 (0 - 331)	2 (50.0%)	1 (25.0%)	1 (25.0%)	509.5 ± 586.5 (4 - 1117)	2 (50.0%)	0 (0.0%)	2 (50.0%)	2 (50.0%)
Worsening Fecal Incontinence	2	205.0 ± 178.2 (79 - 331)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1012.0 ± 148.5 (907 - 1117)	0 (0.0%)	0 (0.0%)	2 (100.0%)	2 (100%)
Defecatory Dysfunction	2	2.5 ± 3.5 (0 - 5)	2 (100.0 %)	0 (0.0%)	0 (0.0%)	7.0 ± 4.2 (4 - 10)	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Treatment-Related AEs: Urinary Problems

AE Cate gory	Total AEs N	Time to Onset				Duration				Unresolved N (%)
		Mean Days	≤ 30 Days	31-120 Days	121+ Days	Mean Days	≤ 30 Days	31-120 Days	121+ Days	
Urinary Problems	**8**	**176.6 ± 336.4 (0 - 947)**	**5 (62.5%)**	**1 (12.5%)**	**2 (25.0%)**	**497.4 ± 533.8 (0 - 1133)**	**4 (50.0%)**	**0 (0.0%)**	**4 (50.0%)**	**5 (62.5%)**
De Novo Incontinence	1	947.0 ± (947 - 947)	0 (0.0%)	0 (0.0%)	1 (100.0%)	906.0 ± (906 - 906)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
Worsening Incontinence	3	155.3 ± 190.6 (0 - 368)	1 (33.3%)	1 (33.3%)	1 (33.3%)	1018.7 ± 141.1 (1861 - 1133)	0 (0.0%)	0 (0.0%)	3 (100.0%)	1 (33.3%)
Other Urinary Problems	4	0.0 ± 0.0	4 (100.0%)	0 (0.0%)	0 (0.0%)	4.3 ± 6.6 (0 - 14)	4 (100.0%)	0 (0.0%)	0 (0.0%)	4 (100.0%)

Treatment-Related AEs: Infections

AE Category	Treatment-Related AEs	Time to Onset			Duration		
		Mean Days	≤ 30 Days	31-120 Days	Mean Days	≤ 30Days	31-120 Days
Infection	25	17.2 ±14.3 (1 - 58)	21 (84.0%)	4 (16.0%)	19.2 ± 22.6 (2 - 117)	22 (88.0%)	3 (12.0%)
Incision Site	9	17.3 ±10.2 (7 - 33)	8 (88.9%)	1 (11.1%)	11.1 ± 5.4 (2 - 20)	9 (100.0%)	0 (0.0%)
Abscess	2	11.0 ±11.3 (3 - 19)	2 (100.0%)	0 (0.0%)	11.5 ± 6.4 (7 - 16)	2 (100.0%)	0 (0.0%)
Other Infections	14	18.1 ±17.3 (1 - 58)	11 (78.6%)	3 (21.4%)	25.4 ± 28.7 (2 - 117)	11 (78.6%)	3 (21.4%)

Adverse Events: Summary

- **Total Treatment-Related AEs - 115**
  - 47.4% Implanted subjects (72/152)
- **Pelvic Area Pain – 50 (43.5%)**
  - 28.3% of Implanted subjects (43/152)
  - 9 Unresolved
- **Pelvic Organ Prolapse - 13 (11.3%)**
  - 5.9 % of Implanted Subjects (9/152)
  - 7 Surgical Interventions (in 6 subject)
  - 7 Unresolved
- **Infections – 25 (21.7%)**
  - 14.5% of Implanted subjects (22/152)

TOPAS System for FI

Benefit

- Responder50Rate
  - 69% at 12 months
  - 53% at 24 months
- Mean FI episodes
  - 21.7 at baseline
  - 9.3 at 12 months
- Wexner score, FIQOL, PFDI-20, PFIQ-7 improved at 12 months

Risk

115 AEs in 72 (47.4%) subjects

- SAEs – 8 (5.3%) subjects
- Surgery – 7 (4.6%) subjects
- Pelvic Area Pain –
  43 (28.3%) Subjects
- Pelvic Organ Prolapse –
  9 (5.9%) Subjects
- Infection – 22 (14.5%) Subjects

Thank You