Brooke Army Medical Center
Institutional Review Board

HUMAN SUBJECTS RESEARCH
PROTOCOL APPLICATION – Part B

1. PROTOCOL TITLE: Incorporation of Mindfulness Exercises to Reduce Anxiety and Pain during Urodynamic Testing: A Randomized Controlled Trial

2. ABSTRACT Urodynamic study (UDS) is a series of tests that evaluate bladder and urethral function. UDS is associated with pain and anxiety due to the invasive nature of the testing. Several interventions have been attempted to reduce the unpleasantness associated with UDS without success. A novel technique that has been shown to reduce chronic bladder pain is mindfulness. We want to study the changes in patient's perceptions of UDS after a mindfulness intervention.

3. OBJECTIVES/SPECIFIC AIMS/RESEARCH QUESTIONS.
The objective of the study is to investigate whether mindfulness techniques improve patient's perceptions of UDS testing.

1. Objective #1-To evaluate changes in anxiety symptoms during UDS testing.
   Hypothesis: anxiety will improve during UDS testing with prior mindfulness intervention.
2. Objective#2- To evaluate changes in pain intensity during UDS testing.
   Hypothesis: pain will improve during UDS testing with prior mindfulness intervention

4. MILITARY RELEVANCE
Pain and anxiety that may be present in UDS impacts the emotional and physical distress experienced by active duty service members and beneficiaries who need testing. The emotional and physical distress can interfere with the accuracy of their diagnosis so that the proper treatment is not administered for their bothersome urinary issues. This may lead the patient to suffer and this may restrict them from vital training, military readiness, or important life events.

5. BACKGROUND AND SIGNIFICANCE
Urodynamic study (UDS) is a series of tests that evaluate the bladder and urethral function. UDS involves placing catheters that are into the bladder and rectum that can be uncomfortable. UDS is conducted by several people during testing and UDS may require an extended amount of time that can further add to the emotional and physical demands. Not surprisingly, UDS has been reported to be associated with anxiety, embarrassment, and pain[1,2].

Several previous techniques to improve patient's perceptions during UDS have been unsuccessful[3-5]. These interventions include lavender oil, music, and an educational video, and have not improved patients' experiences during UDS. Written patient educational material given before UDS testing has mixed results in the literature[3-4].

Mindfulness based stress reduction is a technique that improves coping during stress events. Mindfulness has been shown to reduce anxiety and pain in the chronic pain disorders of the bladder[6]. Mindfulness can enhance, "detached observation" which can aid in reducing subjective negative evaluation of nociceptive stimuli[7]. It has been suggested that mindful meditation enhances self-regulation which is beneficial during physically and emotionally taxing experiences[7]

6. RESEARCH DESIGN
A prospective randomized controlled pilot trial will be conducted from patients that undergo UDS testing. Eligible study subjects that are willing to participate will be accrued from the Urology clinic. Subjects will be consented by the PI. Subjects will be randomized between standard clinic UDS or UDS with mindfulness exercises. Subjects will not be blinded to the intervention or control group, although the physician performing the UDS will be blinded to the allocation of treatment. A power calculation was performed and 30 subjects are required for this study. Assessment or methodology will be from questionnaires after UDS testing. All subjects will be evaluated with an anxiety questionnaire, urodynamic discomfort questionnaire, and pain visual analog scale.

7. RESEARCH PLAN

7.1 Selection of Subjects

7.1.1. Subject Population. The target population includes all adult (DoD beneficiaries) and active duty patients over the age of 18 that are scheduled to have UDS testing. Pregnant women, children, basic trainees or other special populations will not be included.

7.1.2. Source of Research Material.

Source of Research Material	Clinical Purposes(Y/N)	Research Purposes (Y/N)
Anxiety Questionnaire	N	Y
UDS Questionnaire	N	Y
Pain VAS	N	Y

7.1.3. Inclusion and Exclusion Criteria. Inclusion criterion includes adults (DoD beneficiaries and active duty patients over the age of 18-80) scheduled for UDS testing. Diagnosis to include urinary symptoms requiring urodynamic testing are stress urinary incontinence, Mixed urinary incontinence, Urgency urinary incontinence, overactive bladder, urinary retention, and lower urinary tract symptoms.

Exclusion criteria include age less than 18 years, pregnant-as verified by urine or blood sample, have an alteration in neurologic bladder function, or inability to provide informed consent. Condition that will be excluded include neurogenic bladder, Interstitial cystitis, chronic bladder pain, and inability to have urodynamics performed.

7.1.4. Description of the Recruitment and Prescreening Process. The PI will be present at UDS testing and, in the same setting, will identify potential study participants by reviewing their medical record. The PI will recruit potential study participants for enrollment into this study by discussing it with them and reviewing the attached consent. After completion of informed consent, subjects will be enrolled in the study. Subjects will register into the study and entered into randomization as described previously.

7.1.5. Subject Screening Procedures. Pregnancy testing for subjects will the possibility of becoming pregnant which is already routine testing before UDS testing. Patients who, based on medical record or clinic visit, lack capacity to provide informed consent will not be included in the study.

7.1.6. Consent Process. The PI will obtain the informed consent in a private clinic room on the day of the UDS testing. For subjects who wish to participate in the study, informed consent will be obtained at the time of counselling by the PI. Subjects who do not demonstrate the ability to understand or the willingness to sign the written consent document will be excluded from study entry.

7.1.7. Compensation for participation. No compensation or payment to subjects will be made for participation in this study.

7.2 Drugs, Dietary Supplements, Biologics, or Devices.

7.2.1 N/A

7.2.2 N/A

7.3. Study Procedures/Research Interventions. Potential subjects will be invited to participate in this study by the PI, when it is determined that a UDS evaluation is appropriate for their standard treatment. All subjects who agree to participate will be randomized into either the control group or the intervention (mindfulness exercise) group. Randomization assignment will be computer generated at a 1:1 ratio. On the day of their scheduled appointment subjects will present to the Urology Clinic at SAMMC. All subjects will be escorted to an exam room within the Urology Clinic, as per usual protocol, where they will be consented to participate in the study. After consenting to participate, subjects will be asked to complete an initial self-report assessment of state anxiety (see attached). Following completion of the initial state-anxiety assessment, subjects in the control group will be asked to sit alone quietly in the exam room with the lights on, uninterrupted, for 10 minutes. They will be given no other instructions other than to wait in the exam room. Subjects in the intervention group will be lead through a mindfulness exercise in which they will be asked to focus their attention on their breath (see attached script). This exercise will take approximately 10 minutes and will be led by a Clinical Psychologist. Mindfulness exercises facilitate a state of detached observation of the subject's situation and reduce negative physical and emotional stimuli[7]. At the end of the 10 minutes (control) or the completion of the mindfulness exercise (intervention), all subjects will complete a second state-anxiety assessment. Routine UDS evaluation (one catheter in the rectum and one catheter in the bladder) will commence for all subjects. Following completion of the UDS evaluation, subjects will complete a third and final assessment of state-anxiety in which they will be asked to assess their level of anxiety when it was at its highest while undergoing the UDS evaluation.

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Assessment	**Visit / Follow Up (F/U) Interval**		
Study Day / period	1 week before	Procedure	
Informed Consent, discuss Plan, etc.		x	
Randomization		x	
Demographics, History & Physical		x	
Anxiety Questionnaire		x	
UDS Questionnaire		x	
Pain VAS		x	
Self-evaluation Questionnaire		x	

7.3.1 Collection of Human Biological Specimens. N/A

7.3.1.1 Laboratory evaluations and special precautions. N/A

7.3.1.2 Specimen storage. N/A

7.3.2 Data Collection. A de-identified electronic database will be maintained by the PI and associate PIs on a CAC protected computer. Access to the database will be only by study investigators. Database will be password and firewall protected. There will be no transmission of data or external databases.

7.3.3. Human Biological Specimens/Tissue/Data Banking. N/A

Statistical Consideration

7.4 7.4.1 Sample Size Estimation. Based on a sample size calculation, to achieve an alpha of 0.05 with power of 80% sample size should incorporate 25 subjects. After accounting for 15-20% drop out/withdrawal, a total of 30 patients should be enrolled.

Estimate Required Sample Size	**25**
Estimate Participant Drop Out / Withdrawal	**5**
Total Enrollment Requirement	**30**

Enrollment at Each Site	
BAMC	**30**

7.4.2 Primary (i.e., primary outcome variables) and secondary endpoints. The primary outcome is a reduction in anxiety as measured by the anxiety survey. Secondary outcome is a reduction in physical distress as measured by the pain VAS and UDS survey. Secondary endpoints will include self-evaluation questionnaires to assess differences between both groups.

7.4.3 Data analysis. ANOVA will be used to compare the visual analog scale scores between groups. Paired t-test will be used to evaluate the anxiety difference. Chi-squared test will be used to compare self-evaluation categories between both groups.

7.7 Confidentiality. Questionnaires will be de-identified of PII. Data will be entered into the database within 24 hours of collection. Questionnaires will then be stored in a locked cabinet in the Urology Clinic, only accessible by Dr Jellison. Electronic database will be stored on a CAC protected computer within a password protected folder. Only investigators in this study will have access to the electronic database. Upon completion of the study, hard copy data will be archived and secured in a locked cabinet within a locked office. The signed informed consent documents will be retained for 3 years and the signed HIPAA Authorizations will be maintained for 6 years after the date of completion, after which, the files will be destroyed in HIPAA approved disposal container and electronic data will be destroyed through the Information Management Division (IMD) as per SAMMC protocol.

7.7.1 Certificate of Confidentiality. Particularly sensitive information will not be collected.

8.0 RISKS/BENEFITS ASSESSMENT

8.1 Risks. Risks associated with participating in this study are minimal. There is a very slight risk for loss of confidentiality. This risk will be minimized by maintaining data on secure computers. There may be minimal risks to subjects of emotional unease by participating in mindfulness exercises.

8.2 Potential Benefits. Subjects may experience lower levels of anxiety, pain and/or discomfort after undergoing mindfulness exercises.

9.0 ADVERSE EVENTS, UNANTICIPATED PROBLEMS, AND DEVIATIONS

9.1 No adverse events are anticipated. If subjects are not comfortable with the UDS testing, we will stop testing as per standard clinic protocol.

9.2 Reporting Unanticipated Problems Involving Risks to Subjects or Others, Serious Adverse Events and Deaths to the Office of the IRB, BAMC.

All unanticipated problems involving risk to subjects or others, serious adverse events, and all subject deaths related to the study will be reported within 48 hours of the research team's knowledge of the event by phone (210-916-0606), by e-mail (BAMC_IRB_AE@amedd.army.mil), by facsimile (210-916-1650) or via letter addressed to Human Protections Administrator, Office of the Institutional Review Board, Brooke Army Medical Center, Attn: MCHE-CI,3698 Chambers Pass, Fort Sam Houston, TX 78234-6315. A complete written report will follow the initial notification within 10 working days.

9.3 Research Monitor. *N/A*

10.0 WITHDRAWAL FROM STUDY PARTICIPATION. In the event a subject decides to withdraw from the study, the mindfulness exercises will end and the patient will proceed with routine UDS evaluation. There are no consequences to the subject from withdrawing from the study.

11.0 USAMRMC Volunteer Registry Database. N/A

12.0 REFERENCES.

1. Suskind AM, Clemens JQ, Kaufman SR, Stoffel JT, Oldendorf A, Malaeb BS, Jandron T, Cameron AP. Patient perceptions of physical and emotional discomfort related to urodynamic testing: a questionnaire-based study in men and women with and without neurologic conditions. Urology. 2015;85(3):547-51.
2. Yeung JY, Eschenbacher MA, Pauls RN. Pain and embarrassment associated with urodynamic testing in women. Int Urogynecol J. 2014 May;25(5):645-50.
3. Hougardy V, Vandeweerd JM, Reda AA, Foidart JM. The impact of detailed explanatory leaflets on patient satisfaction with urodynamic consultation: a double-blind randomized controlled trial. Neurourol Urodyn. 2009; 2009;28(5):374-9.
4. Stav K, Siegel YI, Beberashvili I, Sella HZ, Zisman A. Provision of information leaflet before urodynamic study reduces the pre-examination anxiety level. Neurourol Urodyn. 2015 Jul 21. [Epub ahead of print]
5. Solomon ER, Ridgeway B. Interventions to decrease pain and anxiety in patients undergoing urodynamic testing: A randomized controlled trial. Neurourol Urodyn. 2015 Jul 30. doi: 10.1002/nau.22840. [Epub ahead of print]
6. Kanter G, Komesu YM, Qaedan F, Jeppson PC, Dunivan GC, Cichowski SB, Rogers RG. Mindfulness-based stress reduction as a novel treatment for interstitial cystitis/bladder pain syndrome: a randomized controlled trial. Int Urogynecol J. 2016 Apr 26. [Epub ahead of print]
7. Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiatry.1982; 4(1):33-47.

13.0 TIME REQUIRED TO COMPLETE THE RESEARCH (including data analysis).
With an estimated accrual of 6 patients per month, participant accrual is estimated at 10 months. Another 2 months would be spent processing data. This results in an estimated study duration of 12 months.

14.0 STUDY CLOSURE PROCEDURES
A Protocol Closure Report will be completed and submitted to the Brooke Army Medical Center IRB upon completion of all data collection, analysis and publications/presentations. The informed consent document will be kept for a minimum of 3 years, and the HIPAA Authorization form will be kept for a minimum of 6 years, following completion of the study at the urology clinic in locked cabinet that is accessible by the PI