PROTOCOL TITLE: Cognitive Behavioral Therapy for Body Image Disturbance in Patients with Surgically-Managed Head and Neck Cancer

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Protocol Revision History

Version Date	Revision Summary
30 October 2017	1.0
19 December 2017	2.0
5 February 2018	3.0

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1.0 Objectives / Specific Aims

Patient-centered oncology care guided by patient-reported outcomes (PROs) is highly prioritized by the American Cancer Society (ACS). Routine use of PROs in cancer care is associated with improved processes of care and patient outcomes. Body image disturbance is a multidimensional construct characterized by a displeasing self-perceived change in appearance and/or function associated with psychosocial distress; it can be assessed using PROs. **Body image disturbance (BID)** is **prevalent**, occurring in more than 75% of head and neck cancer (HNC) patients. It is also a source of **significant morbidity** causing stigmatization, social isolation, and decreased quality of life (QOL). Unfortunately, there is a paucity of data on the topic. Although managing body image concerns is a **key component of HNC survivorship care** according to the ACS, **effective treatments for BID in HNC patients remain unknown.** HNC often requires multimodality therapy including surgery followed by radiation with/without chemotherapy. While many patients consider the toxicity and side effects of chemotherapy prior to treatment, the life-altering morbidity from surgery related to disfigurement, difficulty swallowing, and challenges speaking has not been addressed. As a result, we are unable to deliver optimal patient-centered cancer care. Therefore, the *overarching focus* of this translational program of research is to develop and implement effective, therapeutic interventions for BID. Cognitive behavioral therapy (CBT) is a promising approach to treat BID. However, the effects of CBT on BID in surgically-treated HNC have not been examined. Therefore, the study will evaluate whether a time-limited CBT intervention in the post-treatment time period can address BID in patients with surgically-treated HNC, thereby improving BID and QOL.

Specific Aim: Evaluate the effects of cognitive behavioral therapy on body image disturbance in patients with surgically-treated head and neck cancer.

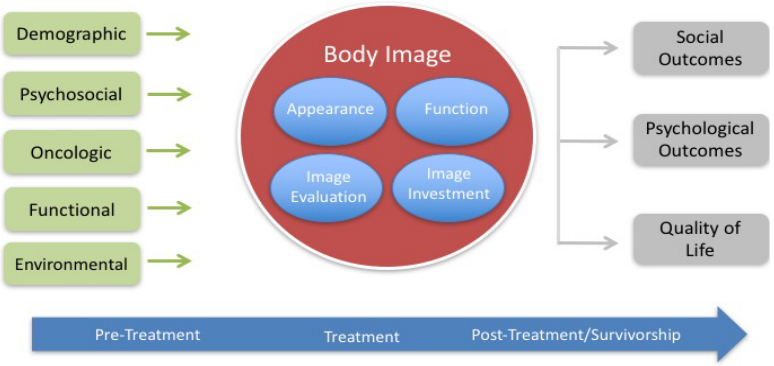
Data from our ongoing research show 85.7% of surgically-treated HNC patients have BID at 1 month postoperatively. 69.6% of these patients report being “likely” or “highly likely” to seek treatment for BID if it were available. Effective treatments for HNC patients with BID remain unknown; however prior work has demonstrated that CBT is an effective intervention for a multitude of psychological and behavioral concerns. Therefore, we will complete a *single-arm, phase II pilot study* of time-limited CBT on BID in patients with surgically-treated HNC. Reliable, validated PRO measures of BID will be collected before, 1 month and 3 months after the CBT intervention to provide preliminary data on the effectiveness of CBT for BID in patients with surgically-treated HNC, addressing this critical knowledge gap. We expect that time-limited CBT implemented in the post-treatment period will decrease BID and improve QOL in affected patients.

2.0 Background

2.a Head and Neck Cancer (HNC) is common, has high mortality, and significant morbidity. HNC is the 6th most common cancer worldwide with 630,000 new diagnoses annually and 350,000 deaths/year[1]. 60,000 patients are diagnosed with HNC annually in the US, causing 12,000 deaths/year[2]. Because HNC arises in cosmetically and functionally critical areas such as the face, tongue, and larynx, there is substantial life-altering morbidity from HNC and its treatment related to disfigurement, difficulty chewing and swallowing, altered smiling, and challenges speaking, with resultant functional and psychosocial impairment and decreased quality of life[3-7].

2.b. Body Image Disturbance (BID) in HNC is due to Disfigurement and/or Dysfunction from HNC and its Treatment. BID is a multidimensional construct characterized by a displeasing self-perceived change in appearance and/or function associated with psychosocial distress[8]. Several conceptual frameworks exist for understanding BID[6,8-13]. One proposes that BID results from both dysfunction and disfigurement with moderating patient, social, and environmental factors influencing the extent of BID over time[6]. Another construct explains body image using image evaluation, the degree to which one is satisfied with one’s appearance, and image investment, the value attached to appearance and physical attributes[14] **(Figure 1)**.

Fig 1. Conceptual Model of Body Image Disturbance



Body image is a multi-dimensional construct based on appearance and function, and evaluation and investment. Demographic, psychosocial, oncologic, functional, and environmental variables are thought to influence body image, which is a dynamic construction that changes over time. Adapted from Rhoten et al[6]

2.c. BID is Common in HNC Patients and has Numerous Deleterious Consequences. Leading organizations such as the Institute of Medicine and Commission on Cancer emphasize the importance of distress in oncology patients[19,20]. BID is a major cause of psychosocial distress for oncology patients[12]. HNC patients are an extremely high risk group, as more than 75% of patients express body image concerns[21,22]. The high prevalence of BID in HNC is attributed to cancer- and treatment-related changes in a highly visible, socially significant part of the body that is integral to self-conception, communication, and interpersonal relationships[6,7,11]. BID results in critical psychosocial impairments, adversely affecting quality of life (QOL) (**Table 1**)[6,11]. It also represents a large unmet need[23], as 69% of HNC patients are dissatisfied with information from clinicians on body image[24].

Table 1. Psychosocial Consequences of BID in HNC Patients[6]	
Increased social isolation[15]	Increased stigmatization[6]
Altered intimacy and relationships[16]	Increased depression[7]
Decreased return to workplace[17,18]	Increased distress[6]

2.d. Patient-Reported Outcome Measures are Critical to Study Body Image in HNC. A Patient-Reported Outcome (PRO) is a report of a patient's health condition originating directly from the patient[25]; they are assessed using validated instruments. PROs are essential to the study of BID due to its subjective, patient-centric nature. PROs are critical for oncology trials[26-29], quality improvement initiatives[30], and comparative effectiveness research[31-34]. Patient-centered oncology care with a focus on PROs is prioritized by major funding, policy making, and regulatory entitles, including the American Cancer Society (ACS) and the National Cancer Institute[28,32,35]. Incorporation of PROs into routine cancer care is associated with beneficial outcomes including survival[36-38]. **PROs are essential to the study of BID; oncology care is enhanced when guided by PROs.**

2.e. Cognitive Behavioral Therapy is an Effective Intervention to Address Body Image Disorders. Cognitive behavioral therapy (CBT) refers to a group of interventions based on the premise that maladaptive beliefs about self and the world contribute to psychological distress and problematic behaviors[39]. Therapeutic strategies that target these maladaptive cognitions by teaching patients to identify and replace these thoughts with more reality-based ones result in symptom reduction and functional improvement[39]. Extensive literature supports CBT protocols to address conditions such as substance abuse, depression, and anxiety[39]. Numerous studies show that stand-alone CBT is effective in treating BID, producing durable treatment gains[40,41].

Innovation:

2.f. Intervention Strategy: Cognitive Behavioral Therapy (CBT) is a Novel Intervention to Treat BID in Patients with HNC. CBT for BID produces decreases in body dissatisfaction and distress and improvements in self-esteem[41]. However, stand-alone CBT for BID has been tested primarily in breast cancer[12,42] or non-oncologic populations[40]. Qualitatively, HNC-related BID differs from other types of BID due to the functional changes following HNC treatment[8]. Data are lacking on effective interventions to treat BID in HNC patients and CBT offers a promising approach. **This study offers a novel intervention to treat BID in HNC patients, filling a knowledge gap and addressing a critical psychosocial need, thereby improving HNC care.**

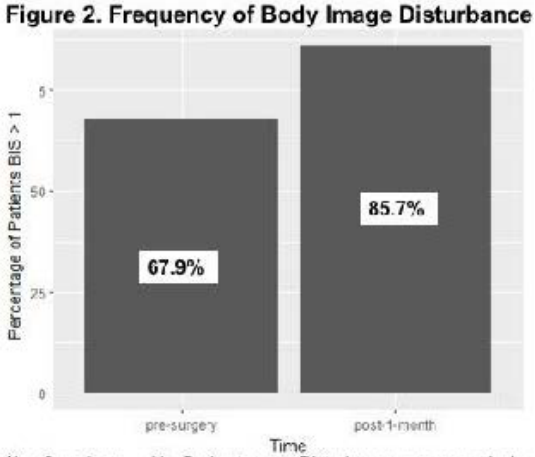
2.g. Methods: Direct-to-Consumer (DTC) Telemedicine is an Innovative Approach to Delivering Psychosocial Services to Rural HNC Patients in South Carolina. We expect that delivery of 5, weekly CBT sessions to HNC patients with BID (**3.b;** CBT intervention) may prove challenging for some patients, as 76.4% of them travel >50 miles to MUSC for their HNC surgery (unpublished data). To overcome this possible travel-related barrier, we propose the innovative solution of offering the ***option*** of a home-based, DTC telehealth platform to deliver CBT to those who cannot travel (**3.b;** telehealth details). Telehealth provides effective behavioral health interventions[43] and is associated with decreased travel burden[44] and increased access to oncology care in rural areas[45]. There is evidence to support that telemedicine CBT is not inferior to face-to-face CBT[46-48]. Our telehealth services will be supported by the Center for Telehealth at MUSC, one of only two centers in the United States designated a Telehealth Center of Excellence[49]. **We will employ existing expertise in telehealth at MUSC to facilitate delivery of CBT to HNC patients with BID who cannot travel for CBT.**

Preliminary Studies:

2.h. Candidate's Academic Background. This proposal builds upon the publications, grants, and clinical expertise of the study team headed by Dr. Graboyes. He is a junior surgeon-scientist with a clinical and translational research program focused on improving patient-centered HNC care. He joined the faculty at MUSC in the Department of Otolaryngology-Head & Neck Surgery as a surgeon-scientist in 2017 and is also an Associate Research member of the Hollings Cancer Center (HCC) Cancer Control Program. During six years of residency and fellowship, he published 32 manuscripts (21 as first author) in the core otolaryngology and oncology journals, gave 5 national presentations, and received 3 internal grants as principal investigator (PI) for HNC projects. During residency, he was the PI of a funded, investigator-initiated single-arm phase II study in which he developed and implemented a perioperative education intervention for patients undergoing total laryngectomy and showed that the intervention has the potential to decrease unplanned readmissions[50]. He also has relevant national leadership roles, serving on the American Head and Neck Society (AHNS) Survivorship, Reconstruction, and Quality Committees. **Dr. Graboyes has a track record of scholarly activity in patient-centered translational HNC research. This proposal utilizes his research and clinical expertise in HNC quality and reconstruction, leverages the world class resources at MUSC and HCC, and facilitates his progression into an independent investigator advancing patient-centered HNC care.**

2.i Candidate's Prior Work: Prospective Cohort Study of BID in Patients with Surgically-Managed HNC. Our ongoing research utilizes a novel prospective cohort study design to characterize the short-term course of BID in patients with surgically-treated HNC using the Body Image Scale (BIS), a validated, 10-item PRO measure of BID in oncology patients[13]. Our preliminary data for patients with at least 1 month of postoperative follow-up (*n*=28) demonstrate that BID is both common and increases over time. 67.9% of patients reported BID preoperatively; this increased to 85.7% at 1 month after surgery (**Figure 2**). In the subset of patients who reported no BID preoperatively, 55.9% developed BID at 1 month after surgery.

Figure 2. Frequency of Body Image Disturbance



% of patients with Body Image Disturbance pre-operatively compared to 1 month postoperatively

We also found that pre-operative PRO measures of depression, social satisfaction, social isolation, shame/stigma were associated with a BIS of ≥ 5 at 1 month after surgery (all $p < 0.05$); but that demographic and oncologic characteristics were not predictive (see **Table 2**).

Table 1: Univariate associations of demographic, oncologic, and psychosocial variables with 1 month post-operative body image scale scores.

		1 month post op BIS < 5 (n = 14)	1 month post op BIS ≥ 5 (n = 14)	
Variable		Summary measure*	Summary measure*	p-value†
Age	median (IQR)	62.5 (53 – 71)	55 (42 – 59)	0.10
Race	White	11 (79)	11 (79)	>0.99
	Non-white	3 (21)	3 (21)	
Sex	Male	12 (86)	8 (57)	0.21
	Female	2 (14)	6 (43)	
Marital status	Married	9 (64)	5 (36)	0.13
	Non-Married	5 (36)	9 (64)	
BMI	median (IQR)	25.5 (21.0 – 26.9)	27.0 (21.2 – 35.7)	0.47
Reconstruction	Free Flap	4 (29)	5 (36)	>0.99
	Non-Free Flap	10 (71)	9 (64)	
Prior Head & Neck Cancer	No	7 (50)	6 (43)	>0.99
	Yes	7 (50)	8 (57)	
Pre-treatment PRO	Anxiety	9 (5 – 11)	10.5 (9 – 13)	0.13
	Depression	4 (4 – 6)	8 (6 – 13)	**0.03**
	Social Satisfaction	20 (16 – 20)	13.5 (9 – 16)	**0.0035**
	Social Isolation	4 (4 – 4)	7 (4 – 12)	**0.0041**
	Shame and Stigma	11 (5 – 14)	19.5 (17 – 34)	**0.0091**

Abbreviations: BIS = Body Image Scale; IQR = inter-quartile range; PRO = Patient-reported outcome
*Summary measures are median (IQR) for continuous variables, and frequencies (percent) for categorical variables.
†Wilcoxon rank-sum test for continuous variables; Fisher's exact test for categorical variables

HNC patients also expressed an interest in seeking treatment for their BID if it were available. Prior to surgery, 63.9% of patients reported that they were 'somewhat likely' or 'highly likely' to obtain treatment for their BID if it were available; this number increased to 69.6% at 1 month after surgery. **Our ongoing research provides novel preliminary data about risk factors for BID following HNC surgery, shows that BID increases in frequency after surgery, and confirms that it represents an area of unmet cancer care need.**

2.j Multidisciplinary Team with Expertise in Survivorship, Patient-Centered Cancer Care, Psycho-Oncology, and Translational Research in HNC. To complement his areas of expertise, Dr. Graboyes has assembled an outstanding multidisciplinary team to improve the feasibility and innovativeness of the proposal (see Biosketches)[51-54]. The team, led by Dr. Sterba, has collaborated on several grants to improve psychosocial and clinical outcomes for HNC survivovors[55,56]. Dr. Day is the Director of the HCC Head and Neck Tumor Program and an experienced HNC translational researcher. As a recent president of the AHNS whose presidential address was entitled, "The Ultimate Constant of Head and Neck Oncology-the physician-patient relationship," he understands the critical importance of patient-centered HNC care[57]. Dr. Maurer is an Instructor of Psychiatry in HCC and Co-Chair of the HCC Psychosocial Distress Steering Committee. Dr. Hill is the Director of Biostatistics for the HCC and has expertise in statistical analysis in translational oncology research. Dr. McElligott is the Medical Director for Telehealth at MUSC. The research team has tremendous experience in translational, patient-centered HNC research, particularly in HNC survivors

3.0 Intervention to be studied

3.a. Development of a CBT Module for HNC Patients with BID. Although extensive literature exists for implementation of disorder-specific CBT[39], no specific CBT modules for HNC patients with BID exist. Therefore a critical initial step is to establish a disorder-specific CBT intervention for HNC patients with BID. In conjunction with Dr. Graboyes, Dr. Maurer will develop a 5-week, CBT module for HNC patients with BID using CBT core components (i.e. psychoeducation, self-monitoring, and cognitive restructuring). The intervention will be informed by existing CBT from other body image disorder realms[40,41]. The intervention

will contain population-specific components including identifying and modifying maladaptive beliefs about disfigurement and functional changes following surgery. It will address the multidimensional nature of BID in HNC patients[6] and will seek to reduce avoidance behaviors, improve social support, and enhance adaptive stress management skills.

3.b. CBT Intervention and Implementation. At the 1-month post-HNC treatment time point, patients with BID as determined by BIS score ≥ 5 will undergo time-limited CBT consisting of 5 weekly sessions. Each session will be guided by the HNC BID module that we develop (**C.2.b.4**) but customized to each patient's specific concerns[40]. Each session will last ~60 minutes and be conducted one-one with Dr. Maurer, who will administer the CBT as part of clinical psycho-oncology care at HCC. Patients will complete questionnaires prior to CBT and 1 and 3 months after CBT (**Figure 4**). We considered alternate dose schedules of CBT but chose a 5-week schedule because evidence suggests that brief (e.g. 5-week) CBT reduces anxiety and depression and improves QOL in cancer patients[58]. To overcome the expected travel distance-related barrier to receipt of CBT (**2.8**), we will offer the ***option*** of home-based, telemedicine CBT through an existing MUSC program[59]. This will consist of one CBT session at HCC followed by iPad-based, tele-CBT for the next 4 sessions. Patients will receive the iPad and brief training session from MUSC Center for Telehealth staff at the in-person CBT session. They will take the iPads home, use them for the next 4 tele-CBT sessions, and mail them back to MUSC at the study conclusion. This strategy, which has been successfully piloted at MUSC[59], addresses the fact that most telehealth usability issues, especially in geriatric patients, occur during initiation[43]. Introducing a second method of delivering CBT (i.e. telehealth CBT vs in-person CBT) will complicate analysis of the effectiveness of CBT by increasing study heterogeneity. However, we expect that this analytic challenge will be outweighed by the increased enrollment related to telehealth CBT for those who cannot travel to HCC for weekly CBT.

4.0 Study Endpoints

4.a. Primary Endpoint

4.a.1. Body Image Disturbance. The primary outcome measure will be BID as measured by the Body Image Scale (BIS). The BIS has been validated in oncology patients[13] and is the most widely used scale for BID in oncology[6]. It is a 10-item measure that is scored on a 4-point Likert scale; higher scores indicate greater body image dissatisfaction. It addresses the affective, cognitive, and emotional aspects of body image[60].

4.b. Secondary Endpoints.

4.b.1. Body Image Investment. Body image investment (i.e. the importance and influence of appearance) will be measured using the Appearance Schemas Inventory-Revised (ASI-R)[61]. This 20-item measure is scored using a 5-point Likert scale with greater scores indicating greater body image investment.

4.b.2. Body Image Coping. The Body Image Coping Strategies Inventory (BICSI) is a validated measure used to assess cognitive and behavioral responses to manage threats to body image[62].

4.b.3. HNC QOL. We will employ the EORTC QLCC30/H&N35 module to evaluate QOL[63].

4.c. Exploratory Endpoints for Mediator Analysis. These following endpoints will be used to determine whether changes in BID over time as measured by the BIS are mediated through these variables. They will also be incorporated into a regression analysis to identify characteristics of sub-populations of patients who benefit from CBT for BID.

4.c.1. Shame and Stigma. The Shame and Stigma Scale is a 20-item, validated tool that measures shame with appearance, stigma, regret, and social/speech concerns in patients with HNC[64].

4.c.2. Depression and Anxiety. Patient-Reported Outcomes Measure Information System (PROMIS) measures of depression and anxiety will be employed. PROMIS measures are validated questionnaire developed by the NIH for evaluating health-related quality of life[65].

4.c.3. Social Roles and Isolation. Social roles and isolation will be assessed by PROMIS measures[65].

4.c.4. Head and Neck Performance Status and Function. Performance Status Scale for Head & Neck Cancer, which assesses performance in domains of eating, speech, and diet[66].

4.d. Exploratory Endpoints to Refine Study Intervention Design, Implementation, and Scalability

4.d.1. Caregiver/Dyad CBT Feasibility Data. We will collect these data for use in future studies based on prior work exploring couples-based CBT in breast cancer patients with BID[67].

4.d.2. Qualitative Assessment of Experience with BID and CBT. To better understand patient experiences with BID not captured in the questionnaires as well as their experiences with CBT, we will perform semi-structured interviews. Participants will be asked to 1) discuss their preferences about the timing, format and content of the CBT sessions 2) describe their program experiences and offer recommendations to improve delivery, and 3) and assess feasibility and acceptability of the intervention. This mixed methods approach will allow for an in-depth exploration of patient experiences[68], help refine the study intervention, and inform intervention implementation for future studies[69].

5.0 Inclusion and Exclusion Criteria/ Study Population

5.a. Study Participants. The study population is adult patients with head and neck cancer undergoing surgery at MUSC with body image disturbance post-treatment.

5.b. Screening for Eligibility. The study team member in collaboration with the electronic medical record and otolaryngology head and neck cancer clinical team, will identify patients ages 18 or older with a pathologic diagnosis of squamous cell carcinoma of the upper aerodigestive tract (oral cavity, oropharynx, hypopharynx, or larynx) or skin of the head and neck presenting for consultation. These patients will be potentially eligible for the study. They will complete a screening BIS questionnaire 1 month after completion of treatment; those with scores $\geq$ 5 will be eligible for the study. Those with scores < 5 will not be eligible for the study, their BIS questionnaire will be shredded, and no personal information about the patient will be saved. The individual data elements from the clinical records that will be accessed in order to identify potential participants for recruitment include:

1. Name
2. Date of birth, to confirm that potential participant is 18 years or age or older
3. Diagnosis of squamous cell carcinoma of the upper aerodigestive tract or skin of the head and neck.

5.c. Inclusion/Exclusion Criteria:

5.c.1. Inclusion Criteria:

- Pathologic diagnosis of squamous cell carcinoma of the upper aerodigestive tract (oral cavity, oropharynx, hypopharynx, larynx) or cutaneous malignancy of the head and neck (e.g. squamous cell, basal cell, melanoma, etc)
- Age $\geq$ 18
- American Joint Committee on Cancer (AJCC) stages I-IV
- Curative intent therapy with surgery with or without adjuvant therapy
- BIS score $\geq$ 5 at 1 month post-treatment

5.c.2. Exclusion criteria:

- Inability to speak English
- Known distant metastatic disease
- Inability or unwillingness of subject or legal guardian/representative to give informed consent

5.d. Inclusion of Women and Minorities. Men and women and members of all races and ethnic groups are eligible for this study.

5.e. Subgroup Distribution: To ensure a reasonable distribution of patients based on potentially relevant characteristics, we will recruit patients diverse by age, race, gender, cancer site, and type of reconstruction.

6.0 Number of Subjects

It is expected that we will enroll 20 subjects in the study.

7.0 Setting

7.a. Study Setting. The primary setting for the study will be the clinic setting at the Head and Neck Tumor Center in the 10th floor of Rutledge Tower or the Hollings Cancer Center.

7.b. Study Sites. This is a single institution study. The only study site is MUSC.

8.0 Recruitment Methods

8.a. Recruitment. Potential participants for the study will be identified after their surgery for head and neck cancer. Recruitment will occur primarily at the Head and Neck Cancer Center on the 10th floor of Rutledge Tower. Participants will be identified via a combination of the electronic medical record and otolaryngology head and neck cancer clinical team. The research coordinator who is screening the clinic schedule for patients will determine whether or not the potential trial participant has consented in EPIC to participate in research studies. For patients who have consented in EPIC to participate in research studies will be contacted by the study coordinator for enrollment. For patients who have not consented in EPIC to participate in research studies, the attending physician for the patient will notify the patient of the study.

8.b. Identification of potential participants. The study team member in collaboration with the electronic medical record and otolaryngology head and neck cancer clinical team, will identify patients ages 18 or older with a pathologic diagnosis of squamous cell carcinoma of the upper aerodigestive tract or skin of the head and neck who are undergoing definitive surgical resection. These patients will be potentially eligible for the study. The individual data elements from the clinical records that will be accessed in order to identify potential participants for recruitment include:

1. Name
2. Date of birth, to confirm that potential participant is 18 years or age or older
3. Pathologic diagnosis of squamous cell carcinoma of the upper aerodigestive tract (oral cavity, oropharynx, hypopharynx, larynx) or head and neck skin

We will call potential participants who have agreed to be contacted about research in EPIC, to discuss the study. For those who have not agreed to be contacted about research in EPIC, we will mail a study recruitment letter prior to their planned clinic visit. If a patient is interested in participating, the coordinator will schedule an in-person meeting to complete screening BIS questionnaire; those with scores $\geq$ 5 will be eligible for the study. Eligible patients after screening who are still interested in enrolling will complete informed consent paperwork in the clinic using protocols from our previous research. The study participants may include patient's of the PI's, but will not be exclusively patient's of the PIs. For potential participants where the PI is not the attending physician and the potential participant has not consented to participate in research per EPIC, then the attending physician for the patient will introduce the study idea to the potential participant. Other than the notification of the study by the attending physician for potential trial participants, the research team will not ask other clinicians to be involved in recruitment. All of the recruitment will be handled by the study coordinator and team.

8.c. Recruitment Materials. A study recruitment letter will be mailed to potential study participants prior to face-face enrollment and informed consent. A copy of the study recruitment letter has been uploaded into eIRB.

8.d. Participant Compensation. Compensation via checks will be provided to participants for the (n=20 participants). The checks will compensate subjects for time, travel, and enrollment. Participants will receive $20 for enrollment and $20 for completion of the study ($20 + $20 = $40/patient x 20 patients = $800).

9.0 Consent Process

Informed consent will be obtained for the study. Those who are interested in enrolling in the study will complete a screening BIS questionnaire. A waiver of written informed consent will be obtained to allow patients to complete the screening BIS questionnaire. Those with scores < 5 will not be eligible for the study, their BIS questionnaire will be shredded, and no personal information about the patient will be saved. Those with BIS $\geq$ 5 will be eligible for the study. For those subjects who are eligible and interested in enrolling, we will describe the elements of the informed consent and HIPAA forms and answer any questions. Subjects will have time to read the informed consent and HIPAA documents on their own. Any additional questions will be answered and then patients will be asked to sign informed consent and HIPAA forms. All participants will receive a copy of their informed consent and HIPAA forms for their records. Separate copies of the documents will be stored in the study binder under each patient's section. Copies of these documents have been uploaded into eIRB.

9.a. Method of Obtaining Consent. Informed consent will occur via face-face discussion between one of the study team members designated to perform informed consent and the potential study participant. The PI, co-investigators, collaborators, and study coordinator will be authorized to obtain informed consent.

9.b. Location of Informed Consent Process. The informed consent process will take place in a private room in the 10th floor Rutledge Tower Head and Neck Cancer Clinic or in Hollings Cancer Center

9.c. Consenting Parties. Only the study participant will provide informed consent. If the participant is not able to consent, the legally authorized representative [LAR] will provide informed consent (and appropriate documentation to substantiate the LAR will be uploaded or verified in EPIC).

9.d. Waiting Period for Informed Consent. Subjects will be allowed up to one month to decide whether or not to participate in the study.

9.e. Coercion and Vulnerable Populations. To prevent coercion, it will be clearly explained to potential participants that participation in the study is completely optional and failure to participate in the study will not adversely affect their clinical care. Only adults will be enrolled in the study. No cognitively impaired adults will be enrolled in the study. Patients who do not wish to participate will not be consented and no identifying information will be collected from them. The document containing their names (previously prepared to permit identification as mentioned above) will be destroyed immediately if they choose to not participate.

10.0 Study Design / Methods

10.a. Study Design. The proposed study is a prospective, single institution, single-arm, phase II pilot study. Cognitive Behavioral Therapy will be implemented into the clinical care of HNC patients at MUSC and HCC. The effects of CBT on body image disturbance will be measured using the Body Image Scale and analyzed using a pre- and post- study design.

10.b. Study Intervention

10.b.1. Development of a CBT Module for HNC Patients with BID. Although extensive literature exists for implementation of disorder-specific CBT[39], no specific CBT modules for HNC patients with BID exist. Therefore a critical initial step is to establish a disorder-specific CBT intervention for HNC patients with BID. In conjunction with Dr. Graboyes, Dr. Maurer will develop a 5-week, CBT module for HNC patients with BID using CBT core components (i.e. psychoeducation, self-monitoring, and cognitive restructuring). The intervention will be informed by existing CBT from other body image disorder realms[40,41]. The intervention will contain population-specific components including identifying and modifying maladaptive beliefs about disfigurement and functional changes following surgery. It will address the multidimensional nature of BID in HNC patients[6] and will seek to reduce avoidance behaviors, improve social support, and enhance adaptive stress management skills.

10.b.2. CBT Intervention and Implementation. At the 1-month post-HNC treatment time point, patients with BID as determined by BIS score ≥ 5 will undergo time-limited CBT consisting of 5 weekly sessions. Each session will be guided by the HNC BID module that we develop, but customized to each patient's specific concerns[40]. Each session will last ~60 minutes and be conducted one-one with Dr. Maurer, who will administer the CBT as part of clinical psycho-oncology care at HCC. Patients will complete questionnaires prior to CBT and 1 and 3 months after CBT (**Figure 3**). We considered alternate dose schedules of CBT but chose a 5-week schedule because evidence suggests that brief (e.g. 5-week) CBT reduces anxiety and depression and improves QOL in cancer patients[58]. To overcome the expected travel distance-related barrier to receipt of CBT, we will offer the *option* of home-based, telemedicine CBT through an existing MUSC program[59]. This will consist of one CBT session at HCC followed by iPad-based, tele-CBT for the next 4 sessions. Patients will receive the iPad and brief training session from MUSC Center for Telehealth staff at the in-person CBT session. They will take the iPads home, use them for the next 4 tele-CBT sessions, and mail them back to MUSC at the study conclusion.

10.b.3. Standardization and Treatment Fidelity. Standardization of intervention administration is critical for study validity and reproducibility. All CBT will be delivered by one psycho-oncologist (SM) with standardized content (regardless of whether the modality is in-person or tele-health CBT). To ensure fidelity of the intervention, the study psycho-oncologist will keep an intervention tracking log which captures data fields such as patient attendance at the session, CBT content delivered, completion of patient homework, technical problems with the session, rating of session length, patient engagement, and patient comprehension (to be completed by psycho-oncologist), and session duration,

10.c. Study Variables

10.c.1 Antecedent Variables.

10.c.1.a Sociodemographics and Oncologic Details. Race, ethnicity, age, gender, marital status, living situation, educational attainment, employment, income level, health insurance, tobacco use, and alcohol consumption will be obtained using questions from the Behavioral Risk Factor Surveillance Survey[70]. Severity of comorbidity will be determined by the Adult Comorbidity Evaluation-27 (ACE-27)[71]. Oncologic and treatment data will be prospectively gathered from the EMR using study-specific questionnaires (date of diagnosis and treatment, tumor site, clinical and pathologic AJCC TNM classification and overall stage grouping, surgery, radiation, and/or systemic therapy treatment details, presence/absence of tracheostomy/laryngectomy, enteral feeding tube, patterns of recurrence, survival, and new primaries).

10.c.1.b. Shame and Stigma. Shame and Stigma Scale is a 20-item, validated tool that measures shame with appearance, stigma, regret, and social/speech concerns in patients with HNC[64].

10.c.1.c. Depression and Anxiety. PROMIS measures of depression and anxiety will be employed. PROMIS measures are validated questionnaire developed by the NIH for evaluating health-related quality of life[65].

10.c.1.d. Social Roles and Isolation. Social roles and isolation will be assessed by PROMIS measures[65].

10.c.1.e. Head and Neck Performance Status and Function. Performance Status Scale for Head & Neck Cancer, which assesses performance in domains of eating, speech, and diet[66].

10.c.2. Outcome Measures

10.c.2.a Primary Outcome Measures.

10.c.2.a.1. Body Image Disturbance. The primary outcome measure will be BID as measured by the Body Image Scale (BIS). The BIS has been validated in oncology patients[13] and is the most widely used scale for BID in oncology[6]. It is a 10-item measure that is scored on a 4-point Likert scale; higher scores indicate greater body image dissatisfaction. It addresses the affective, cognitive, and emotional aspects of body image[60]. A limitation of the BIS as an outcome measure for studies of BID in oncology patients is that there is no validated, clinically meaningful difference in scale scores. This is despite its use in prior studies attempting to characterize the magnitude and prevalence of body image disturbance as a problem in these patients[21,72].

10.c.2.b. Secondary Outcome Measures.
10.c.2.b.1. Body Image Investment. Body image investment (i.e. the importance and influence of appearance) will be measured using the ASI-R[61]. This 20-item measure is scored using a 5-point Likert scale with greater scores indicating greater body image investment

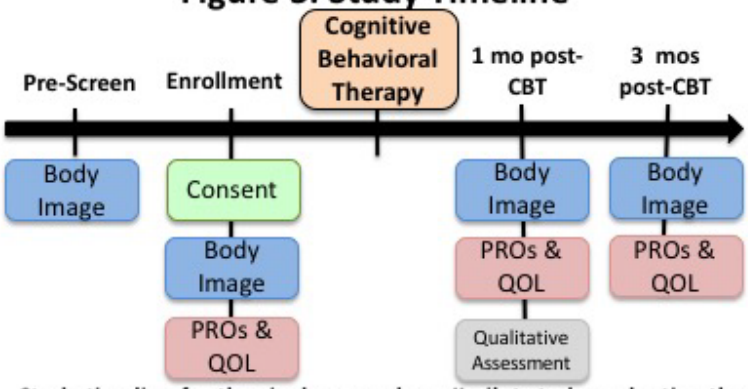
10.c.2.b.2. Body Image Coping. The BICSI is a validated measure used to assess cognitive and behavioral responses to manage threats to body image[62].

10.c.2.b.3. HNC QOL. We will employ the EORTC QLCC30/H&N35 module to evaluate QOL[63].

10.c.2.c. Exploratory Outcome Measures.
10.c.2.c.1. Caregiver/Dyad CBT Feasibility Data. We will collect these data for use in future studies based on prior work exploring couples-based CBT in breast cancer patients with BID[67].
10.c.2.c.2. Qualitative Assessment of Experience with BID and CBT. To better understand the patient experiences with BID not captured in the questionnaires as well as their experiences with CBT, we will perform semi-structured exit interviews. Qualitative methods are essential to allow in-depth exploration of patient experiences[68] and guide intervention development for future studies[69]. Participants will be asked to 1) discuss their preferences about the timing, format and content of the CBT sessions and 2) describe their program experiences and offer recommendations to improve delivery.

10.d. Data Collection:
10.d.1. Data Collection Timeline. The timeline for data collection is shown in **Figure 3**. We have protocols from our ongoing research to obtain data when study time points do not coincide with clinical care.

Figure 3. Study Timeline



Study timeline for the single arm, phase II pilot study evaluating the effects of cognitive behavioral therapy on body image disturbance in patients with surgically-treated head and neck cancer.

10.d.2. Data Collection Instruments. The self-administered PRO measures will be completed by patients electronically using an iPad (or paper format if requested) with assistance from the trained program coordinator as needed. A trained program coordinator will assist with data collection instead of a treating physician to minimize social desirability or attention seeking bias[73]. The data instruments are uploaded into eIRB.

11.0 Data Management

11.a. Data Analysis Plan for Primary Endpoint. The primary endpoint is BIS scores measured at specific time points (Figure 3). We will summarize BIS at each time point by estimating mean and corresponding 95% confidence intervals (CIs), median, standard deviation (SD), inter-quartile range, and range. We will also construct boxplots and spaghetti plots of serially collected BIS scores to provide visual assessment of temporal changes in BIS. Finally, we will analyze BIS scores over time using linear mixed effects (LME) regression models with time as a fixed effect (considered as categorical variable) and subject-specific random effects to account for the correlation among measures obtained from the same subject over time. We will consider transformations for BIS scores to induce approximate normality and stabilize variance. BIS comparisons over time will be conducted using model-based linear contrasts. We will also consider Wilcoxon sign rank tests to compare BIS scores if variable transformations of BIS fail to induce approximate normality. We will not be specifically controlling for telemedicine vs face-to-face CBT but have planned subset analyses to see if differences exist based on method of CBT delivery.

11.b. Power Analysis/Sample Size Justification. Power analyses were performed using PASS 2008, version 08.0.13. Based on our preliminary data, we expect 35 patients/year to be eligible for the study, of

whom 84.6% will be 'somewhat likely' or 'highly likely' to participate in an intervention for their BID (unpublished data). Assuming that we enroll two-thirds of the eligible and 'likely to participate' subjects, if we enroll over 12 months, we would achieve our sample size of n=20.

The study seeks to characterize the effects of CBT on BID. **Figure 4** shows the power to detect absolute differences in BIS for *n*=20 based on a paired t-test with SD (BIS difference) = 3.8 (preliminary data), and two-sided α = 0.05. We estimate power to be at least 80% to detect a difference in BIS scores of

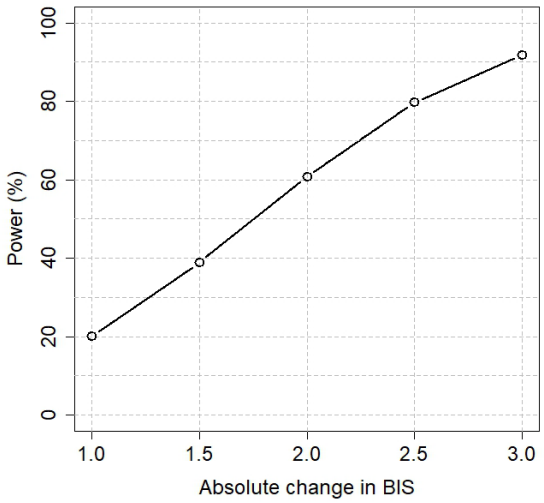


Figure 4: Power to detect change in BIS for a sample size of 20 based on a paired t-test with two-sided α = 0.05 [SD(BIS difference) = 3.8].

approximately 2.5 or greater, a power estimate that is conservative given our proposed analysis plan using LME regression that borrows strength over time. In our preliminary data, we observed BIS differences of approximately 2 points before and after surgery without any intervention. We expect even larger changes in BIS based on the CBT intervention, which is reasonable to provide preliminary evidence of CBT efficacy for our sample of *n*=20.

11.c Data Analysis Plans for Secondary Endpoints.

Sociodemographic and oncologic variables will be summarized using descriptive statistics, including mean, median, standard deviation, interquartile range, and range for continuous variables, and frequencies and percentages for categorical variables.

Additional study variables, including: **shame and stigma scale score** (summed score ranging from 0 to 80); PROMIS measures of **depression**, **anxiety**, **social roles**, and **isolation** (summed scores each ranging from 0 to 16); and **head and neck performance status** (summed score ranging from 0 to 100), will be summarized using descriptive statistics. Additionally, we will evaluate the association between each of these study variables and response to CBT. Specifically, we will examine the association between change in BIS (ΔBIS_1 = 1 month post-CBT versus baseline; and ΔBIS_3 = 3 month post-CBT versus baseline) and each variable using Spearman's correlation coefficient.

Response variables (in addition to [illegible] (summed score ranging from 0 to 80); **body image coping** (summed **l and neck cancer QoL** (summed score ranging from 35 to 140). Des[illegible]marize each variable at each time point. We will also examine the association between change in BIS and each variable using Spearman's correlation coefficient. Finally, we will evaluate the effect of CBT on each response variable using the LME regression model approach described in Section 11.a.

CBT utilization patterns and **caregiver/dyad CBT feasibility data** will be summarized using descriptive statistics.

11.d. Steps to Maintain Confidentiality. To help protect participant confidentiality, we will assign a unique study ID number to each subject's information in place of his/her name and will label data collection forms with the ID number. All hard copy and electronic files will be stored appropriately using double-locked methods and password-protection. Only the study team member will have access to study records. Participant data will be collected and recorded on either a password-protected electronic data capture format (REDCap) or paper-based forms depending upon patient preference. For the paper collection data method, the data collection form will be labeled only with the participant's unique study ID number, and then stored within locked drawers in a locked office. The information on these paper forms will be transferred to a password-protected REDCap database such that all data will be stored in the password-protected REDCap Database. Only members of the study team will have access to the data. We have no plan to use laptops, jump drives, CDs/DVDs to transport data.

11.e Quality Control of Collected Data. The PI will meet with the study coordinator once each month to review the quality of the collected data, assessing for missing data, internally inconsistent data, other data irregularities, progress towards enrollment.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects (if applicable)

12.a.1. Identification of risks and plans to minimize risk.

Expected Risks related to cognitive behavioral therapy	**Frequency**
• Emotional distress/discomfort	☐Occurs frequently, ☐Occurs infrequently X Occurs rarely ☐Frequency unknown
• frustration	☐Occurs frequently, ☐Occurs infrequently X Occurs rarely ☐Frequency unknown

12.a.2. Criteria below under which an individual subject's study treatment or study participation would be stopped or modified. At subject, PI, or study team member request.

12.a.3. Criteria under which the entire study would need to be stopped. Per IRB or PI discretion.

12.a.4. Reporting of subject withdrawals/dropouts to the IRB prior to study completion. Via IRB annual continuing renewal submission.

12.b. Definition of Adverse Events and Protocol Deviations.
12.b.1. Definition of adverse events (AE) for this study. Any undesirable sign, symptom or medical or psychological condition that is related to the study intervention (cognitive behavioral therapy).

12.B.2 Definition of serious adverse event. A serious adverse event will be considered any undesirable sign, symptom, or medical condition which is fatal, is life-threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, constitutes a congenital anomaly or birth defect, is medically significant and which the investigator regards as

serious based on appropriate medical judgment. An important medical event is any AE that may not result in death, be life-threatening, or require hospitalization but may be considered an SAE when, based upon appropriate medical judgment, it may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions of SAEs.

12.b.3 Definition of an unanticipated problem. An unanticipated problem is any event, experience that meets ALL 3 criteria below (*see MUSC IRB policy HRPP 4.7*):

- is unexpected (in terms of nature, severity, or frequency) given: (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

- is related or possibly related to a subject's participation in the research; and

- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

12.b.4 Definition of a protocol deviation. A protocol deviation is any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way without the investigator first obtaining IRB approval (*See MUSC IRB Policy HRPP 4.14*).

12.c. Adverse Event / Unanticipated Problem Recording and Reporting.

12.c.1. Inclusivity of adverse events collection. All AEs described above will be collected and reported.

12.c.2. Method of event data be collection. Data collection will occur via electronic spreadsheet. The information will be saved in REDCap and managed by the study team.

12.c.3. Adverse Event classification. AE classification will occur using NCI Common Toxicity Criteria, Version 4.0.

12.c.4. Relationship of adverse events to study participation. The PI will specify the following relationship of AEs to study participation:

Definite:	AE is clearly related in time and a direct association can be demonstrated to the study intervention
Probable:	AE is reasonably related in time and is more likely explained by the study intervention than by other causes
Possible:	AE may be reasonably related in time and the AE can be explained equally well by causes other than the study intervention

12.c.5. Timing of recording/reporting of adverse events/unanticipated problems. Recording/reporting of AEs will begin after the subject signs informed consent and end after the subject completes the intervention and follow up period as defined in the protocol.

12.d. Data and Safety Oversight Responsibility.

12.d.1 Persons responsible for overseeing safety data. The PI will be responsible for overseeing safety data.

12.d.2. Content of aggregate reviews. Aggregate reviews will occur by the PI for all adverse events, unanticipated problems, protocol violations, audit results, early withdrawals, whether the study accrual pattern warrants continuation/action, and endpoint data.

12.d.3. Timing of aggregate reviews. Aggregate reviews will occur monthly.

13.0 Withdrawal of Subjects

If subjects choose to withdraw from the study, they can do so by completing the withdrawal letter located or as requested from the study investigator. If a participant withdraws from the study for any reason, the research team will be allowed to use previously collected information (e.g. to account for participant's withdrawal from the study in the publication of study flow).

14.0 Risks to Subjects

14.a. Foreseeable risks to subjects. Although the risks of the study are minimal, one risk of participating in this study is that confidential information about the participant may be accidentally disclosed. The likelihood of this risk is low as all the investigators have been involved in similar research in the past and have not experienced this problem before due to adequate safeguards. There are no physical risks to the study participants by joining this study. However, there is the possibility that the study participant may feel uncomfortable or upset talking about cancer or body image concerns. The study participant will be encouraged to take time when answering questions and may refuse to answer any question at any time during this study. The study participant may be asked to provide information considered confidential or private during study interviews. The Study staff will review the medical record. All information captured on paper forms will be stored in a locked cabinet within a locked office to protect confidentiality. Also, electronic data will be stored using password-protected files only accessible by the study team through password-protected servers.

14.b. Unforeseeable risks to subjects. We do not expect any unforeseeable risks with the study.

15.0 Potential Benefits to Subjects or Others

15.a. Direct Benefits to Participants. Extrapolating from data about the effect of CBT on BID in other domains (e.g. breast cancer, non-oncologic BID), it is expected that patients will have decreased BID and improved QOL as a result of CBT[12,41,42], although patients may not receive direct benefit.

15.b. Indirect Benefit to Participants (Benefits to Society): Completion of the study aim is expected to improve the quality of patient-centered cancer care. These data are also expected to provide essential data for further hypothesis generation and facilitate intervention development and implementation. Our novel application of CBT to address BID in surgically-treated HNC will provide essential preliminary data to support a randomized, controlled trial evaluating the effects of CBT on body image disturbance in surgically treated HNC.

15.c Risk/Benefit Analysis for Participants. On the whole, given the minimal risks of the study, the possibility of direct benefit, and the large indirect benefit, we feel that the risk/benefit ratio for potential subjects favors participation in the study.

16.0 Sharing of Results with Subjects

There is no plan to share results of the patient reported outcome measures with the subjects.

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