Brief Guided Mindfulness Meditation for Women Undergoing Stereotactic Breast Biopsy: Effects on Patient Self-Report, EEG Activity, and Physiological Measures

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A Doctoral Dissertation

Presented to

The Faculty of the Department

Of Psychology

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

By

Chelsea Gilts Ratcliff, M.A.

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ABSTRACT

Background: Stereotactic breast biopsies (SBB) are associated with significant anxiety. As anxiolytic medication is not a viable option for many patients, nonpharmacologic methods to manage acute anxiety in this setting are needed.

Method: In this single-blind trial, we examined feasibility and acceptability, as well as the efficacy of guided meditation (GM) compared to guided focused breathing (FB), both delivered for 10 min before and throughout SBB, and standard care (SC), on anxiety and pain ratings, blood pressure, pulse, and brain activity in women undergoing SBB. Patients were recruited prior to SBB and randomized in a 2:2:1 ratio to GM (n=30), FB (n=30), or SC (n=16). Anxiety, pain, blood pressure, and pulse activity were assessed at baseline, after a 10-min pre-SBB group-specific activity (GM, FB, or SC (listening to neutral audio clips)), and post-SBB. Anxiety and pain were also assessed every 4 min during SBB, and electroencephalogram (EEG) activity was collected throughout the study. Baseline trait mindfulness was examined as a moderator of the intervention.

Results: Fifty-four percent (84/157) of eligible patients provided consent for the present study, and 90% (76/84) of consented patients were evaluable. Linear multilevel modeling covarying for baseline anxiety ratings revealed a significant group by time interaction on change in anxiety ratings during the procedure ($p < 0.001$). Women in GM reported a steeper reduction in anxiety during the biopsy compared to FB ($\beta = -0.09$, $p = 0.001$) and SC ($\beta = -0.12$, $p = 0.001$), while FB and SC reported similar reductions in anxiety during biopsy ($p = 0.65$). There were no group differences in pain ratings during the biopsy, and no group differences on any measure after the 10-min group-specific activity or after the biopsy. Moderation analyses indicated that participating in GM buffered the effect of low trait mindfulness on anxiety before and during biopsy and pain after biopsy.

During biopsy, GM had greater delta wave activity in the left primary somatosensory cortex (S1), medial prefrontal cortex (PFC), insula, and bilateral precuneus compared to SC. FB had greater delta activity than both GM and SC in the bilateral S1, anterior PFC, insula, and precuneus, and left medial PFC during biopsy. Further, delta wave activity in the left medial PFC negatively correlated with anxiety, and delta wave activity in the left S1, insula, and precuneus negatively correlated with pain ratings reported during biopsy. Additionally, GM had greater theta wave activity in the right medial and anterior PFC compared to SC. Similarly, FB had greater theta wave activity in the bilateral anterior PFC, right medial PFC, and right insula and compared to SC. Theta activity in these regions was not associated with anxiety or pain ratings during biopsy. Groups did not differ in any other bandwidth during biopsy.

Conclusion: Results indicate GM is a feasible and accepted intervention. Additionally, GM relieves anxiety during biopsy more effectively than FB and SC. Compared to SC, both GM and FB were associated with neuronal quieting (i.e., greater slow-wave activity) in regions associated with pain processing, emotional and cognitive engagement, and self-awareness. Lastly, participation in GM appears to be particularly useful for individuals who report low trait mindfulness, suggesting even transient increases in mindfulness may be beneficial in acutely stressful settings.

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DEDICATION

I would like to acknowledge the many people who made this study, and the exhilarating, challenging experience that came with it, possible. First, I would like to thank my husband, Collin Ratcliff, for his love and support throughout graduate school, and for his endless acceptance and encouragement. I thank my parents and brother, who have been enthusiastic cheerleaders of every undertaking, including this one, throughout my life. I also thank my mentor, Lorenzo Cohen, who truly changed the course of my life and career by graciously giving his time, support, encouragement, and guidance throughout the last four years. I also thank my academic advisor, Peter Norton, for providing mentorship and opportunity to a once-orphaned graduate student. I would also like to acknowledge the members of the Integrative Medicine Program, without whom this project would not have been possible and the past years would not have been nearly so bright: Amy Spelman, Sarah Prinsloo, Alejandro Chaoul, Stephanie Zepeda, Zinat Taiwo, Amie Koronczok, Rosalinda Engle, and Smitha Mallaiah. Lastly, I would like to thank the Cancer Prevention Research and Training Team, especially Drs. Shine Chang and Carrie Cameron, for believing in and funding this project, and for their dedication to ensuring strong mentorship for young investigators.

Brief Guided Mindfulness Meditation for Women Undergoing Stereotactic Breast Biopsy

Each year, up to six percent of all women in the US have inconclusive mammographs warranting further diagnostic testing (Bruening et al., 2009). Many of these patients require large-core needle stereotactic breast biopsy (SBB), an outpatient procedure involving local anesthesia (Meyer et al., 1999). When undergoing SBB, the patient lies prone on a table approximately four feet above ground, with the breast hanging freely through a hole in the table. Unable to see the progress of the procedure, the patient hears a mammography machine guiding the radiologist's instruments to the site and a relatively loud vacuum during tissue removal. Not surprisingly, this procedure is laden with anxiety for most patients due to the uncertain nature of cancer status as well as the foreign, uncomfortable equipment (Lang et al., 2006). Helbich et al. (1996) report that almost one-third of all women desire anxiolytic medication prior to the procedure. Indeed, many women are prescribed sedation or analgesic medication prior to biopsy, but frequently the amounts prescribed are predetermined and there is no consideration of individual patient characteristics (e.g., medication tolerance) in the amount prescribed (Martin, Lennox, & Buckley, 2005). Additionally, taking such medication limits patients from driving or working after the procedure.

This level of procedural distress is uncomfortable, inconvenient, and unhealthy for patients (Cohen et al., 2011; Parker et al., 2009). Patient distress can also contribute to appointment cancelations, incomplete procedures, and longer procedure time due to patient "noncompliance" (Lang, Ward, & Laser, 2010; Schupp, Berbaum, Berbaum, & Lang, 2005). Thus, reducing patient distress has major implications not only for patients, but also for the efficient use of resources during cancer prevention procedures. Nonpharmacological methods to increase

patient comfort and compliance during SBB can contribute to more efficient cancer prevention and treatment at the patient and institutional level.

Self-Hypnosis for Medical Populations

Over the past 10 years, several research groups have examined the impact of self-hypnosis on patient distress when undergoing medical procedures (Flory, Salazar, & Lang, 2007; Montgomery, David, Winkel, Silverstein, & Bovbjerg, 2002; Schnur, Kafer, Marcus, & Montgomery, 2008). Self-hypnosis involves inducing patients into a hypnotic state through deep breathing, guided imagery, and a focus on a floating sensation (Schupp et al., 2005). In a variety of medical populations, including individuals undergoing invasive medical procedures, large core needle breast biopsy, and other outpatient radiology procedures, patients induced into self-hypnotic relaxation during their procedure report significantly less anxiety and pain and request less analgesic medication than controls (Flory et al., 2007; Schnur et al., 2008). Additionally, patients under self-hypnosis are more cooperative with providers and spend less time in the procedure room, which can dramatically reduce costs associated with medical procedures (Lang & Rosen, 2002; Lang et al., 2010), including SBB (Lang et al., 2006). These studies have also demonstrated beneficial physiological responses to self-hypnosis including decreased heart rate, lower blood pressure, and reduced cortisol (Lang et al., 2006; Martin et al., 2005). Thus, self-hypnosis offers nonpharmacologic relief from anxiety and pain during surgery that can be successfully used by patients with no previous hypnosis experience.

Mindfulness Meditation for Anxiety and Pain Reduction: Evidence

Mindfulness-based meditation is another nonpharmacologic approach to distress management that has received considerable attention in recent years and has been applied to both healthy and medical patient populations (Dimidjian & Linehan, 2003; Kabat-Zinn, 2003).

Though one conceptualization of mindfulness-based meditation has not yet been uniformly accepted, most definitions of mindfulness generally highlight *attention* to and *acceptance* of the present moment as core components (Bishop et al., 2004; Coffey, Hartman, & Fredrickson, 2010). Matchim and Armer describe mindfulness-based meditation as "an awareness of moment-by-moment experiences that arises from purposeful attention, along with nonjudgmental acceptance of the experiences" (2007). Interventions focused on cultivating mindfulness have generally yielded large effect sizes ($d \approx .50$) on stress, anxiety, and pain outcomes (Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Matchim, Armer, & Stewart, 2011).

Though traditional mindfulness-based programs, such as Kabat-Zinn's Mindfulness Based Stress Reduction (MBSR; Kabat-Zinn, 2003) or Segal, Williams, and Teasdale's Mindfulness Based Cognitive Therapy (MBCT; 2002), call for relatively extensive training across several months, some studies suggest that as little as one hour of training in mindfulness meditation yields valuable, though transient, decreases in stress and anxiety (Carmody, Reed, Kristeller, & Merriam, 2008; Zeidan, Johnson, Gordon, & Goolkasian, 2010). Eifert and Heffner (2003) demonstrated that just 10 minutes of training in acceptance-based coping significantly decreased avoidance and anxiety in the face of an anxiogenic stimulus (CO_2 rich air) compared to a group that practiced deep breathing. In keeping with the notion that present awareness produces both psychological and physiological benefits, Haythornthwaite and colleagues (2001) found that burn patients undergoing dressing changes reported less physical pain when told to attend to sensory information compared to those instructed to distract themselves. Similar experimental findings have been reported by Erisman and Roemer (2010), Arch and Craske (2006), Campbell-Sills and colleagues (2006), and Gutierrez, Luciano, and Fink (2004), suggesting that less than one hour of training in mindfulness strategies was associated with

reduced self-reported and physiological distress in the face of disturbing or painful stimuli. Though these findings are encouraging, they have not yet been applied to medical or clinical settings. Carmody and Baer (2008) point out that mindfulness training for clinical populations has been limited to those that can commit to relatively extensive training, neglecting many patient groups that may be in great need of such distress management strategies. Patients undergoing SBB fall within this neglected population for mindfulness strategies, as they are typically only aware of their biopsy one to two days in advance. The proposed project will provide an abbreviated form of mindfulness training to SBB patients, providing important information on the feasibility of using brief mindfulness training in populations excluded from longer-term training.

Mindfulness Meditation for Anxiety and Pain Reduction: Theory

Though there is a quickly growing evidence base for the effectiveness of short- and long-term mindfulness-based interventions (Greeson, 2009), there are relatively few studies considering the mechanisms or mediators by which mindfulness works (Black, 2010). Several researcher groups have recognized this deficit, and have put forth their own models describing the way in which mindfulness takes its effect (Baer, 2003; Brown, Ryan, & Creswell, 2007; Coffey et al., 2010; Coffey & Hartman, 2008; Hölzel et al., 2011; Shapiro, Carlson, Astin, & Freedman, 2006). Though each of these theorists favors different terminology, all include two core constructs in their characterization of mindfulness: present-moment attention (e.g., intentional observation of stimuli in the present moment) and acceptance (e.g., a non-judgment attitude towards one's internal and external experience). Additionally, though these theories propose a wide variety of mechanisms of action, there are two proposed mechanisms common to most models: 1) exposure to unpleasant stimuli and 2) cognitive flexibility, or the ability view

one's experience objectively (Baer, 2003; Brown et al., 2007; Hölzel et al., 2011; Shapiro et al., 2006).

Hölzel states that practitioners of mindfulness "meet unpleasant emotions by turning toward them, rather than turning away" and find that this practice counter-intuitively reduces unpleasant internal reactions and fosters an increased sense of well-being (2011; p. 545). This process of intentionally "turning toward" threatening internal or external stimuli is very similar to exposure therapy described in the cognitive-behavioral literature. Exposure involves attending to, rather than suppressing or avoiding, unpleasant or feared internal or external stimuli with the goal of habituating to that stimuli, which reduces the emotional reaction and urge to avoid the stimuli (Chambless & Ollendick, 2001). Exposure, even in brief applications, has been repeatedly shown to reduce anxiety and avoidance behaviors (Barlow & Craske, 2003; Hindo & González-Prendes, 2011; Norton & Price, 2007; Raes, Koster, Loeys, & De Raedt, 2011), and has been suggested as a primary mechanism of action for cognitive-behavioral therapy and other efficacious psychotherapies (Foa, 2011).

Empirical studies corroborate the notion that mindfulness decreases distress via prolonged exposure. Baer (2003) points out that the first published study of MBSR (Kabat-Zinn, 1982) encouraged chronic pain patients to "focus careful attention directly on the pain sensations" and accompanying cognitions and emotions (p.128). Baer notes that this resulted in desensitization to the pain, enabling patients to experience pain without the accompanying emotional distress (2003). Similarly, Shapiro (Shapiro et al., 2006) notes that MBCT (Segal et al., 2002) encourages participants with chronic depression to attend to negative emotions and thoughts, and posits that this resulted in more adaptive, less avoidant, responses to negative affect, thereby reducing relapse of major depressive disorder. Relatedly, Linehan and colleagues

recommend providing mindfulness in the form of Dialectical Behavior Therapy (DBT; 2006) to individuals suffering from borderline personality disorder. Linehan notes that mindfulness requires practitioners to attend to both positive *and* negative emotions, which reduces fear of negative emotions and allows practitioners to respond more adaptively to unavoidable fluctuations in mood. Further, brief experimental studies providing less than one hour of mindfulness training to novice meditators indicate that mindfully attending to noxious stimuli including violent film clips (Erisman & Roemer, 2010), gruesome photos (Arch & Craske, 2006), CO_2 enriched air (Eifert & Heffner, 2003), burn pain (Haythornthwaite et al., 2001) and electrical shocks (Gutiérrez et al., 2004) resulted in reduced distress in the face of such stimuli, providing further evidence that the salutatory effects of mindfulness may be due to exposure and habituation.

Increased cognitive flexibility, or the ability to take a decentered, nonjudgmental perspective on one's experience, is another mechanism by which mindfulness may make its effect. The major mindfulness-based therapy programs including MBSR (Kabat-Zinn, 2003), MBCT (Segal et al., 2002), and DBT (Lynch et al., 2006) encourage mindfulness practitioners to adopt the perspective of a nonjudgmental observer on their own experience. Shapiro (2006) posits that this "decentered" perspective "affords a different place from which to view the present moment" which allows practitioners to respond to the present moment with greater flexibility, as they are not constrained by automatic emotional reactions (p. 381). Brown, Ryan, and Creswell echo this, stating that practicing mindfulness prompts perceptual flexibility, enabling practitioners to recognize that "all consciously perceived phenomena, including thoughts and feelings are insubstantial in nature; thoughts become 'just thoughts,' feelings 'just feelings,' rather than necessarily accurate reflections of reality" (2007; p.226). Teasedale, Segal,

and Williams (1995) point out that this "meta-cognitive" way of thinking is in direct opposition to rumination, and allows individuals to acknowledge ruminative thoughts, let them go without emotional fanfare, and direct their attention back to stimuli in present moment. Additionally, Hölzel points out that this "meta-cognitive awareness" leads to recognition that all things, including unpleasant things, are impermanent and are not cause for emotional reactivity (2011). There are clear parallels between the cognitive flexibility described in the mindfulness literature and the cognitive restructuring discussed in the cognitive-behavioral literature. Like the cognitive flexibility described above, cognitive restructuring is a method by which one acknowledges automatic subjective reactions, examines these reactions as a third party might, and develops a more objective perspective, rooted in reality rather than based on one's own emotionality (Beck, 1970). Thus, mindfulness may reduce distress via mechanism very similar to those proposed in cognitive behavioral therapy: 1) exposure and habituation to internal and external stimuli and 2) cognitive flexibility regarding internal and external stimuli.

Unfortunately, there is limited research empirically testing mediators of mindfulness, and there has been no research testing mediators of brief mindfulness interventions. Carmody and colleagues (2009) sought to test the mechanisms of action proposed by Shapiro (2006) and found that, though exposure as measured by the Acceptance and Action Questionnaire (AAQ; Bond et al., 2008) increased following an 8 week Mindfulness Based Stress Reduction (MBSR) intervention, changes in AAQ scores did not mediate the effects of MBSR on psychological distress. However, the effect of MBSR on psychological distress was partially mediated by cognitive flexibility (as measured by the Scales of Psychological Well-being (SPWB) Environmental Mastery subscale; Ryff, 1989). Carmody used an 8-week long MBSR intervention to test mediators of mindfulness, making the relationship of her findings to brief

mindfulness-based meditation difficult to ascertain, as mechanisms of action for brief mindfulness provided to novice meditators may be quite distinct from those in advanced meditators (Tang & Posner, 2013).

Nevertheless, in light of the theoretical support for exposure and cognitive flexibility as mediators of the anxiolytic and analgesic effects of mindfulness, it is proposed that participating in brief mindfulness meditation before and during biopsy will reduce patients' anxiety through: 1) continued exposure to patients' internal and external state which will lead to habituation and 2) encouraging patients to adopt an objective, decentered perspective on the internal or external stimuli she experiences.

Though there is considerable overlap in the aims of mindfulness and hypnosis interventions, the methodology, theory, and potential mechanisms of action of the two approaches are distinct. The self-hypnosis literature provides empirical evidence that nonpharmacologic relief from anxiety and pain during surgery and can be provided to patients who are unable to dedicate time to training. However, the present project seeks to build upon the currently developing theory underlying mindfulness meditation as well as to extend the basic laboratory research on brief mindfulness meditation to a patient population. Additionally, the proposed study will include multimodal assessment of anxiety and pain through self-report, physiological measures (e.g., blood pressure and pulse), and electroencephalogram (EEG) activity, potentially providing valuable information for understanding how mindfulness-based meditation interventions impact pain and anxiety.

Multimodal Assessment: EEG Activity and Mindfulness Meditation

The relatively recent advent of brain imaging techniques makes identifying the neurological underpinnings of experience a fascinating and important possibility. Measurement

of brain activity using techniques such as EEG, MRI, fMRI, and PET has been reported in a number of studies assessing both novice and expert mediators (see Chiesa & Serreti, 2010 for review). There are several powerful advantages to using EEG to image meditation-associated brain activity compared to other imaging techniques. For example, EEG equipment is significantly lower in cost, more tolerant of participant movement, and relatively portable, enabling it to be used in diverse settings. One disadvantage of EEG is relatively poor spatial resolution, making it difficult to ascertain the activity taking place in deep brain structures, such as the amygdala. Additionally, though the data on the brain's electrical activity supplied by EEG is arguably richer than the blood-oxygen-level (BOLD) supplied by fMRI, interpreting the complex data gathered via EEG requires a significant amount of effort and expertise. Nonetheless, several research groups have begun to examine the effects of meditation on the brain's electrical activity using EEG. Such studies typically examine the effect of meditation on electrical activity broken into five traditional frequency bandwidths in the brain (Frei et al., 2001): Delta (< 4 Hertz (Hz)), Theta (4-7 Hz), Alpha (8-12 Hz), Beta (13-32 Hz), and Gamma (> 30 Hz). A brief overview of frequency bandwidth's association with meditation follows.

Delta, the slowest frequency band, is associated with deep, slow-wave sleep and has also been associated with inhibition of activity in brain regions (Niedermeyer & Lopez da Silva, 1993). Tei (2009) found greater resting state delta wave activity in experienced Qigong practitioners compared to controls in the medial prefrontal cortex, somatosensory cortices, and precuneus, all areas associated with attention and sensory processing. Similarly, Faber and colleagues found that experienced Zen meditators exhibited greater delta wave activity in the medial prefrontal cortex compared to nonmeditators (2008). Both these studies associated the increased delta wave activity as indicative of inhibition of emotional and cognitive engagement,

or "detachment" as described in meditation traditions (Cahn & Polich, 2006). To the best of our knowledge, no studies have reported on delta wave activity associated with novice meditation.

Theta wave activity, associated with transitioning from wake to sleep, increased relaxation (Jacobs & Friedman, 2004), and sustained attention (Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999) has also been found to increase during meditation, even for novice meditators (Aftanas & Golocheikine, 2001; Fell, Axmacher, & Haupt, 2010). Mindfulness meditation appears to increase frontal lobe theta compared to concentrative meditation (Dunn, Hartigan, & Mikulas, 1999). Further, meditation-related increases in frontal theta wave activity have been correlated with self-reported feelings of bliss and low thought content (Aftanas & Golocheikine, 2001; Hebert & Lehmann, 1977).

Increased alpha wave activity over the frontal lobes has been also associated with self-reported relaxation, and has been found to increase during meditation for both novice and expert meditators (Fell et al., 2010; Takahashi et al., 2005), though not all studies have found this effect (Cahn & Polich, 2006; Jacobs & Lubar, 1989). Further, a considerable amount of research indicates that meditation induces greater alpha asymmetry in the frontal lobes, with alpha activity (like delta) assumed to be *inversely* related to cortical activity (e.g., lower left-relative-to-right alpha activity is associated with greater left-relative-to-right cortical activity; Coan & Allen, 2004). Studies combining EEG and fMRI support this inverse association, with increases in alpha associated with decreased blood flow (Goldman, Stern, Engel, & Cohen, 2002; Sadato et al., 1998), and stimulation of brain regions via sensory input associated with decreased alpha (Başar, Schürmann, Başar-Eroglu, & Karakaş, 1997; Schürmann & Başar, 2001). Additionally, lower left-sided alpha activity (i.e., greater left-sided cortical activity) in the frontal lobes is associated with positive, approach-oriented emotions, while lower right-sided alpha activity (i.e.,

greater right-sided cortical activity) is associated with emotions associated with withdrawal (Coan, Allen, & McKnight, 2006; Davidson et al., 2003). Further, lower left-sided alpha activity in the frontal and temporal lobes has been shown to follow mindfulness training (Davidson et al., 2003; Keune, Bostanov, Hautzinger, & Kotchoubey, 2013; Moyer et al., 2011). Thus, one may expect that participation in guided meditation may result in greater total alpha, as well as greater frontal alpha asymmetry, with lower left-compared-to-right alpha activity.

Increases in the higher frequency bandwidths of beta and gamma appear to only occur in advanced meditators. For example, yoga meditators in practice for over 20 years exhibited greater beta and gamma wave activity during meditation practice compared to yoga meditators in practice for less than four years (Thomas, Jamieson, & Cohen, 2014). Similarly, long-term meditators have greater gamma wave activity when resting and during active meditation compared to controls (Banquet, 1973; Fell et al., 2010; Lutz, Greischar, Rawlings, Ricard, & Davidson, 2004). Interestingly, high frequency activity in non-meditators has been associated with threat processing, worry, and negative affect (Oathes et al., 2008).

Though the neurological changes resulting from any form of meditation, particularly in novice meditators, are far from clear (Cahn & Polich, 2006), previous research suggests that participation in brief mindfulness mediation may result in increased theta wave activity, increased alpha activity and frontal asymmetry, and potentially increased delta activity compared to controls. Additionally, brief guided mindfulness meditation will not likely result in changes in higher frequency bandwidths such as beta or gamma.

Present Study

The present study had five aims. The *primary* aim was to determine the acceptability and feasibility of conducting a guided mindfulness meditation (GM) while women are undergoing

SBB. We hypothesized that the GM will be feasible and that participants would find the intervention acceptable and a positive experience. Specifically, we hypothesized that over 50% of eligible patients would elect to participate, and at least 80% of the consented patients would comply with the study protocol.

The *second* specific aim was to conduct an initial evaluation of the effect of GM compared to FB and SC on self-reported anxiety in participants undergoing SBB. We hypothesized that women who participated in the GM group would report a steeper reduction in anxiety during SBB, and lower anxiety before and after SBB compared to women in FB and SC. We also hypothesized that the women in the FB group would report a steeper reduction in anxiety during SBB, as well as lower anxiety before and after SBB, compared to women in SC.

The *third* specific aim was to examine the effect of GM compared to FB and SC on self-reported pain during SBB and blood pressure (SBP, DBP and pulse) before and after SBB. We hypothesized that participation in the GM group would be associated with a steeper reduction in pain during the SBB, and lower pain, blood pressure, and pulse before and after SBB compared to participation in FB and SC, with the FB group having favorable outcomes relative to the SC group.

The *fourth* specific aim was to compare EEG activity of participants in GM to participants in FB and SC during biopsy. We expected an association between group and EEG activity in brain regions previously implicated in studies examining anxiety and mindfulness. Specifically, we expected that those in GM would experience greater activity in the low frequency bands of delta, theta, and alpha (associated with decreased or inhibited cortical activity) in regions associated with pain processing and emotional and cognitive engagement compared to those in FB and SC, with FB having favorable outcomes relative to SC. To limit the

number of analyses conducted with the EEG data, we selected five regions of interest (ROIs): the primary somatosensory cortex (S1), medial and anterior prefrontal cortex (PFC), insula, and precuneus. Additionally, where there are group differences in ROIs, we examined the correlation of each frequency band with VAS anxiety and pain ratings reported during biopsy (e.g., if groups differ in delta wave activity in the medial PFC, we examined the correlation of delta wave activity in the medial PFC with VAS anxiety and pain during biopsy). Based on the previously reported literature, we expected that low frequency activity (i.e., delta, theta, and alpha) in each ROI would be negatively associated with self-reported anxiety and pain. We expected that in this group of novice meditators, groups would not differ in high frequency band activity (i.e., beta and gamma).

Lastly, the *fifth* specific aim was to explore baseline psychosocial factors as moderators of the effects of the intervention. Though exposure and cognitive flexibility were outlined above as the proposed mediators of the GM intervention, unfortunately, the present study is limited in its ability to empirically examine mechanisms of GM's effects. Due to the necessarily brief amount of time each participant had to complete questionnaires before and after their biopsy, mediational models examining potential mechanisms of the intervention was not feasible. However, the present study did examine *for whom* GM was most effective. We hypothesized that individuals higher in pre-treatment levels of trait mindfulness would benefit more from the intervention. Support for this moderation model has been demonstrated by Shapiro and colleagues who found that individuals higher in the Mindfulness Attention Awareness Scale (Brown & Ryan, 2003) benefited more from MBSR (2011). Furthermore, *attention* to and *acceptance* of the present moment have been proposed as the two core components to mindfulness, and structural equation models suggest that the *observing* and *nonjudgment*

subscales of the Five Facets of Mindfulness Questionnaire (FFMQ; Baer, 2006) map onto these two constructs, respectively (Coffey et al., 2010). Thus, we hypothesized that individuals with higher baseline scores on the *observing* and *nonjudgement* subscales of the FFMQ would derive greater benefit from GM than women with lower scores on the observing and nonjudgement subscales who undergo GM. We also conducted exploratory analyses examining the other subscales of the FFMQ (i.e., describing, awareness, and nonreactivity) as moderators of the intervention's effect.

METHOD

Participants

Participants were 84 women scheduled for a SBB at MDACC. To be included patients had to be 18 years or older, right hand dominant, able to understand and read English, sign a written informed consent, and be willing to follow protocol requirements. Women who had a documented diagnosis of a formal thought disorder (e.g., schizophrenia), or obtained a score of 3 or below on the Six-Item Cognitive Screener were excluded from the study.

Potential study participants were scheduled for SBB in the Breast Diagnostic Clinic (BDC) in the MDACC Diagnostic Radiology Department. A research assistant regularly consulted the ClinicStation schedule for the BDC, and telephoned patients scheduled for SBB. Over the telephone, the research assistant determined interest and basic study eligibility, including an assessment of cognitive impairment with the Six-Item Screener (Callahan, Frederick, Hui, Perkins, & Hendrie, 2002). The research assistant provided patients with information about the study, stating that the study is assessing "two different forms of relaxation training during SBB." The research assistant described the EEG procedure and the type of

questionnaires the participant would be asked to complete. Interested and eligible participants agreed to come to MDACC 90 minutes prior to their scheduled SBB. Two hours of participant's parking expenses at MDACC were paid.

Procedures

Ninety minutes prior to their scheduled biopsy, a research assistant met with each participant to obtain informed consent. Participants then completed baseline assessments including a 20 minute-long battery of questionnaires, vital signs, and a 5 minute assessment of eyes-closed EEG activity using a 23 lead Midstar system.

The participant was then randomized to GM, FB, or SC in a 2:2:1 fashion, with 2 participants assigned to GM and FB groups for every 1 participant assigned to SC. A form of adaptive randomization (minimization) was used because this was a small study and simple randomization could result in covariate imbalances (Pocock, 1983). Statistical adjustment of covariates can take imbalances into consideration, but results are generally more credible when they are obtained from groups with comparable baseline distributions. In minimization, group assignment is done sequentially. Before a participant is assigned to a treatment group, the number of already randomized participants with similar covariate characteristics is totaled. The totals are computed based on marginal sums so that each covariate is considered separately. The treatment assignment for a participant is then based on which assignment would produce the best overall balance with respect to the covariate characteristics. Minimization is similar to stratification in that participant characteristics are used to assign participants to the treatment conditions. In this study, the participant characteristics used for group assignment were age, menopausal status, Breast Imaging and Data System (BI-RADS) category used to describe

mammogram findings, patient awareness of BI-RADS category, and whether patients are on medications with possible anxiolytic effects.

After randomization, a mind-body specialist trained in both interventions guided GM and FB participants in the respective program for 10 minutes prior to the SBB, following a standardized script based on previously efficacious brief mindfulness studies (Erisman & Roemer, 2010) and guidance from Alejandro Chaoul, Ph.D. Participants assigned to SC listened to a selection of neutral-content audio clips from National Public Radio for 10 minutes. EEG activity was recorded throughout the 10-minute period. Vital signs and brief self-report measures, including an intervention expectation assessment for patients in FB or GM, were obtained just after the 10-minute period. Pre-biopsy GM and FB sessions were audio recorded, and 10% of these recordings were randomly selected and reviewed to ensure quality and fidelity of pre-SBB GM and FB sessions.

At the time of the biopsy, the patient entered the clinic room with the EEG leads remaining in place. A research assistant reconnected the leads to the EEG machine once the patient was in the prone position on the biopsy table. For participants assigned to GM or FB, the mind-body specialist was stationed near the participant's head when she was on the biopsy table. Using a standardized script, the mind-body specialist guided GM and FB participants through their assigned interventions throughout the procedure. Participants in SC received standard care by typical radiology staff throughout the procedure. All participants were asked to close their eyes throughout the procedure to enable EEG data interpretation. The research assistant monitoring EEG data acquisition asked all participants to report their pain and anxiety on a verbal assessment scale ranging from 0-10, every 3-5 minutes (Benotsch, Lutgendorf, Watson, Fick, & Lang, 2000). EEG assessment was collected continuously throughout the procedure.

When the procedure concluded, the participant exited the procedure room with the research assistant. Five minutes of post-biopsy eye-closed EEG activity was recorded. The EEG cap was then removed and the research assistant obtained vital signs and administered a 5-minute battery of self-report.

Guided Mindfulness Meditation Group. The guided mindfulness meditation was based on previously efficacious brief mindfulness based meditation studies (Eifert & Heffner, 2003; Erisman & Roemer, 2010). Mind-body specialists with extensive experience were trained and available to lead both the intervention and control conditions in accordance with the scripts developed for the study. The GM intervention began by instructing participants to attend to their breath, simply noticing their breathing as it was occurring in the present moment. Participants were told that attending to their breath could be a helpful anchor to the present moment, if they notice their thoughts being carried away into worries about the past or future. Next, GM participants were instructed to direct their attention to other sensations they were experiencing in the present moment (e.g., the feel of the chair supporting them, fabric of clothing on the skin, sounds in the room), and encouraged to notice those sensations as a third party might, without judging them as good or bad, simply accepting them as part of the present moment. Finally, participants were encouraged to notice any internal sensations (e.g., feelings such as anxiety, worry, or regret), labeling them as appropriate (e.g., “anxiety”, “worry”, or “regret”) and gently turning their attention back to the present moment, using their breath to anchor themselves back in the present if needed. Participants were reminded throughout the session that a wandering mind is natural, and were encouraged to be aware of mind wandering and gently, nonjudgmentally return their attention to the present moment.

Focused Breathing Control Group. This active control group focused on slow diaphragmatic breathing. Focused breathing control groups are commonly used in mindfulness studies, as they allow participants to be blinded to condition (Arch & Craske, 2006; Eifert & Heffner, 2003; Erisman & Roemer, 2010). Though focusing on the breath is a popular method for stress management (Carmody et al., 2008), it lacks the moment to moment nonjudgmental awareness that is integral to mindfulness meditation. Thus, comparison of GM to FB enables us to examine impact of meditation over and above that of relaxation through focused breathing.

Standard Care Group. Prior to biopsy standard care participants listed to neutral NPR clips. During biopsy, MDACC Breast Diagnostic Clinic staff provided patients standard care, including warning patients of upcoming stimuli, encouraging patients to remain calm, and generally expressing empathy to patients.

Measures

Recruitment and Participation Tracking Data. To determine the acceptability and feasibility of participating in this study, tracking data was kept on interest in participation during the recruitment period, and completion of questionnaires before and after the intervention.

Patient Satisfaction Survey. Patient satisfaction with the study was assessed after the procedure. Patients rated how useful patients found the program, how able they felt to follow the program, whether they would participate in the program again, and whether they would recommend the program to a friend.

Patient Expectation Survey. Patient expectation of the intervention was assessed before randomization for all participants and after the 20 minute pre-SBB training period for participants in GM and FB. Patients were asked to rate how useful they expect the guided relaxation to be in relieving anxiety and pain during SBB using a 0 (not useful at all) to 4 (very

useful).

Verbal assessment scale of anxiety (Anxiety VAS) is frequently used to assess anxiety trajectory throughout a medical procedure (Flory et al., 2007) and is considered a reliable descriptor of the anxiety experience (National Institutes of Health, 1987). Patients provided a rating from 0-10, with a rating of 0 indicating ‘‘no anxiety’’ and 10 indicating ‘‘worst possible anxiety’ at baseline, after the 10 minute pre-biopsy group specific activity, every 3-5 minutes during the biopsy, and again immediately after biospy (Benotsch et al., 2000).

Speilberger State/Trait Anxiety Inventory. Current and general anxiety was assessed using the Speilberger State/Trait Anxiety Inventory (STAI; Spielberger, 1970). The STATE scale (Form Y-1) is a 20-item scale that provides information about a person’s current level of anxiety. The TRAIT scale (Form Y-2) is a 20-item scale that provides information about a person’s general anxiety. Respondents rate frequency of feelings or symptoms using a 4-point Likert-type scale with the responses “almost never,” “sometimes,” “often,” and “almost always.” There is extensive normative data using this scale. It is widely used in research on diseased and healthy populations, and it has good internal consistency reliability (0.85-0.95; Smith & Lay, 1974). All study participants completed the full Speilberger State/Trait Anxiety Inventory at baseline, and completed the STATE scale after the 10 minute pre-biopsy group specific activity, and then again immediately after the biopsy.

Verbal assessment scale of pain (Pain VAS) is considered the single most reliable descriptor of the pain experience (National Institutes of Health, 1987). Patients provided a rating from 0-10, with a rating of 0 indicating ‘‘no pain” and 10 indicating ‘‘worst possible pain” at baseline, after the 10 minute pre-biopsy group specific activity, every 3-5 minutes during the biopsy, and again immediately after biospy (Benotsch et al., 2000).

Brief Pain Inventory. The Brief Pain Inventory (BPI-Short Form) is a validated, widely used, self-administered questionnaire to assess severity of pain and impact of pain on daily functioning among patients (Cleeland, 2006). Item 1 assesses whether or not patients are currently experiencing pain other than minor headache, sprain, or toothache. Item 2 allows patients to indicate on a whole body diagram the exact location of pain. Items 3-6 measure severity of pain on a 0-10 numeric scale. Item 7 assesses current treatment and item 8 assesses relief from pain treatments or medications within the last 24 hours. Finally, item 9 includes 7 subratings regarding the impact pain within the previous 24 hours has had on patients' QOL. The BPI was administered at baseline and immediately after SBB.

Blood Pressure and Heart Rate. Diastolic and systolic blood pressure and pulse was taken at baseline, after the 10 minute pre-biopsy group specific activity, and immediately after SBB.

EEG Activity. Changes in neuromodulation was assessed using a 23 channel EEG digitally recorded using Mitstar amplifier, with the 10/20 system of electrode placement to address when, where, and to what extent modules of neuronal networks become active during baseline, pre-biopsy, biopsy, and post-biopsy time points. The electrodes detect electrical discharges that occur as a result of activity from brain cells. The earlobes and inion were utilized for reference and ground electrodes Skin were prepped using Nu-prep skin cleanser and electrodes were held in place with impendence adjusted to less than 5Kohms, using Electro-paste electrode gel. EEG activity was recorded for 5 minutes at baseline, throughout the 10 minute pre-biopsy group specific activity (i.e., GM, FB, or listening to NPR), continuously throughout the biopsy, and for 5 minutes after the biopsy has concluded. To increase ease of interpretation, all EEG activity will be recorded with patients' eyes closed. EEG data was processed through low

resolution brain electromagnetic tomography (LORETA) software (Pascual-Marqui, Michel, & Lehmann, 1994), which has been validated with fMRI (Cannon et al., 2012) and PET (Oakes et al., 2004) localization methods, and has been determined to be reliable method to characterize brain activity over time (Cannon et al., 2012).

Five Facet Mindfulness Questionnaire. Trait mindfulness was assessed with the 39-item Five Facet Mindfulness Questionnaire (FFMQ), which is broadly used in mindfulness literature to determine nonjudgmental awareness of present moment experience (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006). This instrument is based on a factor analytic study of five independently developed mindfulness questionnaires, which yielded five factors of mindfulness: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. This measure has been developed as a reliable and valid comprehensive instrument for assessing different aspects of mindfulness in community, student, and clinical samples, with alpha coefficients ranging from .73 to .91 (Bohlmeijer, Peter, Fledderus, Veehof, & Baer, 2011). Additionally, the facets are moderately intercorrelated, indicating that though the facets are related, they represent distinct aspects of mindfulness. Participants completed the FFMQ at baseline.

Medical Markers, Treatment and Risk Factors. Menopausal status; time since suspicious mammogram or ultrasound; SBB complications; total duration of SBB procedure; duration of biopsy; and other background information was obtained from medical records.

Data Analyses

The analyses of the study was conducted in two phases, the first being the descriptive feasibility and process evaluation and the second being the outcome analyses.

The *first specific aim* was to determine the acceptability and feasibility of incorporating a

guided mindfulness meditation program to reduce self-reported anxiety in patients undergoing SBB. Based on previous research examining acceptability of behavioral interventions, it was *a priori* determined that the trial would be considered successful if over 50% of eligible patients participate and at least 80% of the consented patients complete the sessions and all the measures for the study. Additionally, chi-square tests were conducted on the patient satisfaction surveys to determine the percent of individuals in GM and FB who felt the program was useful, were able to follow the program instruction, would participant in the program again, and would recommend the program to a friend.

Before conducting the inferential procedures to examine Aims 2 through 5, extensive descriptive analyses of variables were conducted. First, variable distributions were examined within and across groups in order to assess for the outliers. The boxplot method was used to detect outliers on all medical, demographic, and self-report variables. Analyses conducted with and without outliers revealed no differences in outcome, with one exception: length of biopsy and pulse after biopsy. Two participants' biopsies were determined outliers based on the length of their biopsy (>35 minutes) using the boxplot method. Further, the medical team informed both of these participants that there was difficulty finding any calcifications, noting that their biopsy was taking longer than usual. Thus, these two participants were excluded from analyses based on their unusual biopsy experience. Otherwise, results are presented with outliers on all other variables included. The Kolmogorov-Smirnov test of normality was used for continuous variables, and the skewness and kurtosis of the variables were examined. As anticipated, VAS anxiety and pain scores were not normally distributed, but were skewed to the right with relatively few reports in the highest response categories. To correct for this, we collapsed rating categories of 8, 9, and 10, creating a 0-8 VAS rating scale (Lang et al., 2006). This affected <7%

of the anxiety data and < 5% of the pain data. Levene's test of homogeneity of variance (Levene, 1960) determined that the variances in the three groups were equal.

Bivariate associations between the outcome measures and demographic and disease-related variables, including age, ethnicity, race, employment status, marital status, education, income, menopausal status, anxiolytic medication use, BIRADS category, time since diagnosis, number of cores obtained, previous cancer diagnosis, and previous SBB were evaluated using Pearson product-moment correlation coefficients, chi-square, or analyses of variance where appropriate. Age, BIRADS category, race, ethnicity, and marital status interacted with time to predict VAS anxiety ratings during biopsy (all p-values < 0.005), and education interacted with time to predict VAS pain ratings during biopsy ($p = 0.0003$). Specifically, older age was associated with a steeper reduction in anxiety during biopsy; Caucasian women (n = 56) reported a steeper reduction in anxiety compared to Asian (n = 4) and Black/African American (n = 8) participants; Hispanic/Latina women (n = 13) reported steeper reduction in anxiety during biopsy compared with NonHispanic/Lantina women (n = 70) and women who provided their ethnicity (n = 70) reported steeper reduction in anxiety compared to women who did not (n = 6); widowed participants (n = 6) reported a steeper reduction in anxiety compared to divorced (n = 10) and married (n = 53) participants, and married participants reported a steeper reduction in anxiety compared to divorced participants. Finally, women with BIRADS of 1 (n = 2) or 2 (n = 1) reported steeper reductions in anxiety compared to women with all other BIRADS classifications. Women with graduate degrees (n = 11) reported a steeper reduction in pain during biopsy compared to women who did attend high school (n=2).

With the exception of ethnicity (which was balanced among groups), results did not differ when the above described covariates were included in the model compared to when they were

not. Further, when those who did not provide ethnicity were removed from analyses, results did not differ from when ethnicity was entered as a covariate. Thus, results are presented with ethnicity and the baseline level of the respective outcome variable entered as the only covariates. Medical and demographic variables did not differ by group.

To address *Aims 2 and 3*, the PROC MIXED procedure in SAS (Littell, Milliken, Stroup, Wolfinger, & Schabenberger, 2006) was used to conduct linear multilevel modeling (LMM) analyses testing group differences in *change in* VAS ratings from the first rating of the biopsy throughout the procedure (i.e., the group x time interaction effect on VAS anxiety and pain), controlling for ethnicity and for the baseline VAS rating of the respective outcome measure. A two-level LLM can take the dependent nature of nested longitudinal data (i.e., VAS reports nested within participants) into account and efficiently handles unbalanced designs and missing data without excluding participants or imputing values (Gibbons et al., 1993; Gibbons, Hedeker, Waternaux, & Davis, 1988). Time during biopsy was examined as a quadratic term in the LLM, and was maintained in the model when significant. Additionally, a general linear model (PROC GLM) was used to test for group differences in anxiety, pain, blood pressure, and pulse at specified points in time (e.g., immediately after group-specific activity and after biopsy), controlling for ethnicity and the respective baseline measure.

To address *Aim 4*, low resolution brain electromagnetic tomography (LORETA) was used to examine group differences in activity in five specified ROIs (i.e., S1, medial PFC, anterior PFC, insula, and precuneus) averaged across time during biopsy. LORETA is a method of EEG analysis that can localize electrical activity in both cortical and deeper brain structures based on scalp potentials from a multiple surface electrodes (Congedo, Lubar, & Joffe, 2004; Jensen, Hakimian, Sherlin, & Fregni, 2008). Each patient's EEG recording was visually inspected,

artifact rejected, and processed through the LORETA software program. The LORETA frequency band analysis was done after Frei et al. (2001), with the following five bandwidths: Delta (< 4 Hz), Theta (4-7 Hz), alpha (8-12 Hz), beta (13-31 Hz), and gamma (32-60 Hz). LORETA functional images were computed for each subject and condition separately in each of the five frequency bands. The differences in brain electric activity between groups were assessed by exceedence proportion tests performed on LORETA images of pairwise t-statistics, corrected for multiple testing (Friston, Frith, Liddle, & Frackowiak, 1991). Significant differences in ROIs were determined if groups significantly differed on a voxel falling within the Brodmann area (BA) and Talirach coordinates associated with each of the five a priori ROIs (S1 (BA 3), medial PFC (BA 9), anterior PFC (BA 10), precuneus (BA 7), and insula (BA 13)), Additionally, the activity of each frequency band in each ROI was entered into SAS, where activity was correlated with VAS anxiety and pain ratings reported during biopsy.

Aim 5 involved an *a priori* hypothesis that high scores on the *observing* and *nonjudgement* subscales of the FFMQ will be associated with greater benefit from the GM intervention compared to individuals who report low scores on the *observing* and *nonjudgment* subscales. To address Aim 5, these two subscales were separately added as a predictor to each of the LMMs and GLMs described above to examine Aims 2 and 3. In the LLMs, we tested for an interaction effect of these two FFMQ subscales with group and time in predicting VAS anxiety and pain reported during biopsy. In the GLMs, we will test for an interaction effect of these two FFMQ subscales with group in predicting VAS anxiety and pain reported before and after biopsy. Exploratory analyses will also be conducted to examine potential interaction effects of the other three FFMQ subscales (describing, awareness, nonreactivity) with group on VAS anxiety and pain before, during, and after biopsy.

Power Analyses. Although the primary endpoint was feasibility, group differences in anxiety, pain, blood pressure, pulse, and EEG activity were examined. Randomization was done at a 2:2:1 rate, with 2 patients assigned to GM and FB groups for every 1 participant assigned to SC. Using G*Power, it was determined that 30 patients per intervention group and 15 patients in SC (N=75) who completed 5 repeated measurements during biopsy would enable us to detect a small effect size ($f^2 > 0.05$) for the group-by-time interaction effect in mixed model repeated measure analyses with 95% confidence with 80% power. It was also determined that this sample size would enable us to detect a medium effect size ($f^2 > 0.14$) for the group main effect in a general linear model at specified time points (Faul, Erdfelder, Lang, & Buchner, 2007).

RESULTS

Sample Characteristics

Two-hundred and thirty-five women were contacted via telephone; 78 were ineligible, 73 refused, and 84 were consented and randomized (54% of eligible patients; GM = 34; F*B* = 33; SC = 17; Figure 1). Reasons for ineligibility included being unable to arrive 90 minute before their scheduled biopsy (n = 41), planned benzodiazepine use (n = 9), lack of English proficiency (n = 8), left hand dominance (n = 1), failure of cognitive screening test (n = 1). Initial exclusion criteria also precluded women from participating who had previously been diagnosed with cancer (n = 14) or undergone an SBB (n = 4); however, these criteria were eliminated 1 month after the start of data collection in order to increase accrual rates. Reasons for refusal included declining due to the time commitment (n = 19) and lack of interest (n = 54). Many refusals were due to discomfort with participating in EEG data acquisition, though specific numbers on this were not recorded. Of the 34 women randomized to GM, 4 patients were determined

inevaluable: 2 patients were informed there was difficulty finding any calcifications and their biopsy time was determined outliers by the boxplot method (>35 minutes), 1 patient reported local anesthetic did not work, and jumped several times during the biopsy, and 1 patient did not complete the biopsy due to a scheduling error. Of the 33 women randomized to FB, 3 patients were determined inevaluable: 2 patients refused post-randomization due to a desire to take benzodiazepines, and 1 patient's biopsy was cancelled. Of the 17 women randomized to SC, 1 patient was determined inevaluable due to her biopsy being cancelled. Thus, analyses were conducted on a total of 76 participants (YG = 30; FB = 30, SC = 16). Demographic and medical characteristics are summarized in Table 1. The three groups were similar on all medical, demographic, and baseline self-report variables (Table 2).

Out of the 34 women randomized to GM, 6 did not provide EEG data: 2 participants refused EEG at the time of biopsy, 2 participants had hair extensions preventing the use the gel used in EEG acquisition, 1 participant was allergic to the EEG gel, and 1 participant did not complete the study due to a scheduling error. Of the 28 remaining women in GM who provided EEG data, 8 provided evaluable EEG data. Out of the 33 women randomized to FB, 11 did not provide EEG data: 7 refused EEG at the time of biopsy, 2 participants experienced EEG equipment failure during biopsy, 1 participant had hair extensions preventing the use of EEG gel, and 1 participant withdrew from the study post-randomization. Of the 22 remaining women in FB who provided EEG data, 13 provided evaluable EEG data. Of the 17 women randomized to FB, 4 did not provide EEG data: 2 refused EEG at the time of biopsy, and 2 participants had hair extensions preventing the use of EEG gel. Of the 13 remaining women in FB who provided EEG data, 5 provided evaluable EEG data. Thus, analyses involving EEG data were conducted on a total of 26 participants (YG = 8; FB = 13, SC = 5). There were no differences in medical,

demographic, baseline self-report variables, or anxiety and pain reported during and after biopsy between those who provided EEG data and those who did not, or between those whose EEG data were and were not evaluable.

Aim 1: Feasibility and Acceptability

The primary aim of the present study is to determine the acceptability and feasibility of conducting a guided mindfulness meditation (GM) while women are undergoing SBB. We hypothesized that over 50% of eligible patients will elect to participate and at least 80% of the consented patients will comply with the study protocol. Fifty-four percent (84/157) of eligible patients elected to participate and provided consent for the present study, and 90% (76/84) of consented patients were evaluable. Participants reported similar expectation of intervention usefulness at baseline (GM: M = 3.10, SD = 0.98; FB: M = 2.97, SD = 1.00; SC: M = 3.13, SD = 1.30) at post-group-specific activity (GM: M = 3.23, SD = 0.82; FB: M = 3.28, SD = 0.80) regardless of group. Chi square analysis of patient responses on the satisfaction survey revealed that more women in the FB found the program useful or very useful (96.67%) compared to women in GM (76.67%; χ^2=5.19, p = 0.02). Additionally, there was a trend for more women in FB to indicate they would participate in the program again (96.67%) compared to GM (83.33%, p = 0.09). Women in GM (83.33%) and FB (90%) reported comparable ability to follow the instructions provided by the mind-body specialist (p = 0.58), and the vast majority of women in GM (93.33%) and FB (100%) indicated that they would recommend the program to a friend (p = 0.2).

Aim 2: Intervention Effect on Anxiety Ratings

We hypothesized that women in the GM group would report a steeper reduction in anxiety during the biopsy compared to women in the FB and SC groups, and women in the FB

group would in turn report greater reduction in anxiety compared to women in the SC group. LMM analyses were used to examine group, time, and group by time interaction effects on change in VAS anxiety ratings from the first rating of the biopsy during the procedure, covarying for ethnicity and baseline VAS anxiety. Time during biopsy was examined as a quadratic term in the LLM, and was maintained in the model, as it was significantly associated with change in VAS anxiety scores from the first rating during biopsy ($F_{(1,220)} = 8.48$, $p = 0.004$). Though there was no main effect of group ($F_{(2,220)} = 1.61$, $p = 0.202$), there was a significant group by time interaction ($F_{(2,220)} = 7.94$, $p < 0.001$) on change in VAS anxiety scores from the first rating during biopsy. Specifically, women in GM reported a steeper reduction in anxiety during the biopsy compared to FB ($\beta = -0.093$, $p = .001$, Cohen's d = -0.48) and SC ($\beta = -0.107$, $p = 0.001$, Cohen's d = -0.45), while FB and SC reported similar reductions in anxiety during biopsy ($p = 0.65$, Cohen's d = -0.062; Table 3; Figure 2).

Additionally, we hypothesized that women who participated in the GM group would report lower anxiety (VAS and STAI-STATE) before and after SBB compared to women in the FB and SC groups, while women in the FB group would report lower anxiety before and after SBB compared to women in the SC group. General linear analyses controlling for ethnicity and baseline VAS anxiety revealed no group differences in VAS anxiety ratings after the group-specific activity, at the first rating during the biopsy, and after the biopsy (Table 2). However, there was a main effect of group on VAS anxiety reported at the last rating during biopsy ($p = 0.005$), with pairwise comparisons indicating that women in GM ($p = 0.005$) and FB ($p = 0.002$) reported lower anxiety compared to women in the SC group. There were no group differences in STAI-state anxiety at any time point.

Aim 3: Intervention Effect on Pain Ratings, Blood Pressure, and Pulse

We hypothesized that women in the GM group would report a greater reduction in pain during the biopsy compared to women in the FB and SC groups, and women in the FB group would in turn report greater reduction in pain compared to women in the SC group. LMM analyses were used to examine group, time, and group by time interaction effects on change in VAS pain ratings from the first rating of the biopsy during the procedure, controlling for ethnicity and baseline VAS pain. Time during biopsy was examined as a quadratic term in the LLM, and was maintained in the model, as it was significantly associated with change in VAS pain scores from the first rating during biopsy ($F_{(1,219)} = 9.74$, $p = 0.002$). There was no main effect of group ($F_{(2,219)} = 0.23$, $p = 0.80$) or the group by time interaction ($F_{(2,219)} = 0.11$, $p = 0.89$) on change in VAS pain scores from the first rating during biopsy (Table 3; Figure 3).

Additionally, we hypothesized that women who participate in the GM group will report lower pain (VAS and BPI), SBP, DBP, and pulse before and after SBB compared to women in the FB and SC groups, while women in the FB group will report lower pain, SBP, DBP, and pulse before and after SBB compared to women in the SC group. General linear analyses controlling for ethnicity and the baseline level of the outcome variable revealed no group differences in VAS pain ratings after the group-specific activity, at the first and last ratings during the biopsy, and after the biopsy (Table 2). Additionally, there were no group differences on the BPI, though there was a trend for a main effect of group on average pain reported on the BPI post-biopsy ($p = 0.09$), with pairwise comparisons suggesting women in GM may report less pain compared to women in SC after the biopsy ($p = 0.03$). There were no group differences in SBP, DBP or pulse at any time point.

Aim 4: Intervention Effect on brain activity

We hypothesized that those in GM would experience greater activity in the low

frequency bands of delta, theta, and alpha, and no difference in the higher frequency bands of beta and gamma in ROIs (S1, medial and anterior PFC, insula, and precuneus) during biopsy compared to those in FB and SC, with FB having favorable outcomes relative to SC. Additionally, we hypothesized that low frequency activity (i.e., delta, theta, and alpha) in each ROI would be negatively associated with self-reported anxiety and pain during biopsy.

Delta. Pairwise comparisons of delta activity in each ROIs can be seen in Table 4, and correlations of delta activity in ROIs with anxiety and pain ratings can be seen in Table 5. GM had greater delta wave activity in the left S1 (Figure 4a), left medial PFC (Figure 6a), left insula Figure 9a), and bilateral precuneus (Figure 12a) compared to SC (p's < 0.05). FB had greater delta activity than both SC and GM in the bilateral S1 (Figure 4b-c), bilateral anterior PFC (Figure 8b-c), bilateral insula (Figure 9b-c), bilateral precuneus (Figure 12b-c), and left medial PFC (Figure 6b-c; p's < 0.05). Additionally, FB had greater delta activity than SC in the right medial PFC (p's < 0.05). Delta wave activity in the left medial PFC negatively correlated with anxiety ratings during biopsy (Figure 7; p = 0.03). Additionally, delta activity in the bilateral S1 (Figure 5), left insula (Figure 10), and left precuneus (Figure 12) negatively correlated with pain ratings during biopsy (p's < 0.04).

Theta. Pairwise comparisons of theta activity in each ROI can be seen in Table 6, and correlations of theta activity in ROIs with anxiety and pain ratings can be seen in Table 7. GM had greater theta wave activity in the right medial (Figure 13a) and anterior (Figure 14a) PFC and a trend toward greater right insula theta activity (Figure 15a) compared to SC (p's < 0.05). FB had greater theta wave activity in the right medial PFC (Figure 13b), bilateral anterior PFC (Figure 14b), and right insula (Figure 15b) compared to SC (p's < 0.05). GM and FB did not differ in theta wave activity in any ROI. Theta activity was not significantly correlated with

anxiety or pain ratings during biopsy.

Alpha, Beta, and Gamma. GM, FB, and SC groups did not significantly differ from one another in any ROI in alpha, beta, or gamma bandwidths. Thus, correlations of alpha, beta, and gamma activity in each ROI with anxiety and pain ratings during biopsy were not conducted.

Aim 5: Trait Mindfulness as a Moderator of the Intervention

We first examined whether group assignment interacted with the *observing* and *nonjudgment* facets of mindfulness on the FFMQ and time (i.e., minute during biopsy) to predict VAS anxiety or pain scores reported during biopsy. As in the previous mixed model analyses, change in VAS ratings from the first rating of the biopsy during the procedure was the outcome measure. There was a significant group x time x observing interaction effect on change in VAS anxiety during biopsy ($F_{(2,217)} = 3.16$, $p = 0.044$; Figure 16a). We decomposed the interaction according to high (1 SD above the mean, n = 14) and low (1 SD below the mean, n = 9) observing scores to determine whether group interacted with time during biopsy differently for those with high and low trait mindful-observing. For those with high observing scores, there was a significant group by time interaction ($F_{(2,21)} = 4.27$, $p = 0.03$), with women in GM reporting a steeper reduction in anxiety compared to those in FB ($\beta = -0.20$, $p = 0.01$), and the reduction in anxiety reported by women in SC did not differ from that of GM or FB. For women who reported low observing scores, group did not interact with time to predict change in anxiety rating during biopsy ($p = 0.44$). Nonjudgement did not moderate the effect of group x time on VAS anxiety or pain ratings during biopsy.

We then examined whether the other three facets of mindfulness (describing, awareness, and nonreaction) moderated the effect of group x time on VAS anxiety or pain ratings during the biopsy. There was a significant group x time x nonreaction interaction effect on change in VAS

anxiety during biopsy ($F_{(2,217)} = 4.58$, $p = 0.011$; Figure 16b). We decomposed the interaction according to high (1 SD above the mean, n = 12) and low (1 SD below the mean, n = 13) nonreaction scores to determine whether group interacted with time during biopsy differently for those with high and low trait mindful-nonreaction. For those with high nonreaction scores, there was a significant group by time interaction ($F_{(2,43)} = 6.25$, $p = 0.004$), with women in GM reporting a steeper reduction in anxiety compared to those in FB ($\beta = -0.19$, $p = 0.001$), and a trend toward a steeper reduction in anxiety compared to SC ($\beta = -0.08$, $p = 0.2$). Additionally, women with high nonreaction scores in SC reporter a steeper reduction in anxiety compared to FB ($\beta = -0.11$, $p = 0.05$). Similarly, there was a significant group by time interaction ($F_{(2,34)} = 4.82$, $p = 0.014$) for women with low nonreaction scores, with those in GM reporting a steeper reduction in anxiety compared to those in FB ($\beta = -0.23$, $p = 0.005$), and a trend toward a steeper reduction in anxiety compared to SC ($\beta = -0.33$, $p = 0.1$). For women with low nonreactive scores, reductions in anxiety during biopsy did not differ between SC and FB. Describing and awareness mindfulness facets did not moderate the effect of group x time on VAS anxiety or pain ratings during biopsy.

Next, we examined whether group assignment interacted with the *observing* and *nonjudgment* facets of mindfulness on the FFMQ to predict VAS anxiety and pain scores reported at discreet time points (i.e., after group specific activity and after the biopsy) using GLM. There was a significant group x nonjudgment effect on VAS pain reported after the biopsy ($F_{(2,66)} = 4.92$, $p = 0.011$). Women in GM and FB reported similar pain following the biopsy, regardless of their baseline level of nonjudgment, while higher nonjudgement was associated with lower pain for women in SC (Figure 17a). In other words, GM ($\beta = 0.58$, $p = 0.04$) and FB ($\beta = 0.50$, $p = 0.003$) buffered the negative relation between nonjudgment and pain

reported after the biopsy compared to SC. Observing did not moderate the effect of group on VAS anxiety or pain ratings after group specific activity or after the biopsy.

We then examined whether the other three facets of mindfulness (describing, awareness, and nonreaction) moderated the effect of group on VAS anxiety or pain ratings after group specific activity or after the biopsy. There was a significant group x awareness effect on VAS Pain reported after the biopsy ($F_{(2,66)} = 4.81$, $p = 0.012$; Figure 17b). Specifically, women in GM and FB reported similar pain following biopsy, regardless of their baseline level of awareness, while higher awareness was associated with lower pain for women in SC (Figure 17b). In other words, GM ($\beta = 0.55$, $p = 0.03$) and FB ($\beta = 0.53$, $p = 0.004$) attenuated the negative relationship between awareness and pain reported after the biopsy that was seen in SC. There was also a significant group x nonreaction effect on VAS anxiety reported after the group specific activity ($F_{(2,66)} = 4.39$, $p = 0.017$; Figure 17c). Specifically, women in GM and FB reported similar anxiety following biopsy, regardless of their baseline level of nonreaction, while higher nonreaction was associated with lower anxiety for women in SC (Figure 17c). In other words, being in GM ($\beta = 0.81$, $p = 0.05$) or FB ($\beta = 0.77$, $p = 0.004$) attenuated the negative relationship between nonreaction and anxiety reported after the group specific activity compared to SC. Describing did not moderate the effect of group on VAS anxiety or pain ratings after group specific activity or after the biopsy.

DISCUSSION

Acceptability and Feasibility

The primary aim of the study was to determine the acceptability and feasibility of conducting a guided mindfulness meditation (GM) while women are undergoing SBB. Results

indicated that such an intervention is, indeed, acceptable to patients, as 54% of eligible patients elected to participate and provided consent for the present study. Additionally, results suggest that the intervention was feasible, as 90% (76/84) of consented patients completed the study protocol and were considered evaluable. Interestingly, though more women in FB (97%) compared to GM (77%) indicated that the program was useful, and slightly more indicated they would participate again (GM: 83% vs. FB: 97%), the women reported similar ability to follow the instructions for both interventions (GM: 83% vs. FB: 90%). Though some studies indicate that participants report greater satisfaction following brief mindfulness interventions (Haythornthwaite et al., 2001), that is not always the case. Eifert and Heffner found that, despite the superiority of brief mindfulness training compared brief diaphragmatic breathing training in on fear and avoidance behaviors, participants rated diaphragmatic breathing as slightly more helpful than mindfulness-based acceptance (2003). Nonetheless, it is noteworthy that the large majority of women in both GM and FB reported high rates of satisfaction.

When considering the present study's recruitment rate as a proxy for GM acceptability, it is important to note that the requirement of having to undergo an EEG likely reduced the recruitment rate. Women were asked to arrive at the hospital 90 minutes before their biopsy, a requirement that was in part due to the need to set up and acquire EEG data, which took approximately 20-30 minutes. Over half (53%) of women were ineligible due to appointments preventing them from coming to the study location 90 minutes before biopsy, despite self-reported interested in participating. Additionally, during recruitment women were informed that EEG acquisition requires gel to be applied to the scalp, which remains in the scalp until washed with water. Though women were offered a complementary hair wash/style at the MD Anderson Beauty Shop following their biopsy, few women opted to take advantage of this due to time

constraints. Perhaps, not surprisingly, a significant portion of refusals were due to discomfort with undergoing an EEG before and during biopsy, though specific numbers on this reason for refusal were not documented. Without the inclusion of the EEG data acquisition, it is likely that patient acceptance would be considerably higher than the 54%, possibly on par with the 70-80% acceptance rate reported by similar acute mind-body interventions (Lang et al., 2000; Lang et al., 2006).

Mindfulness Meditation Caused Greater Reductions in Anxiety during Biopsy

Results indicated that women in GM reported a steeper reduction in anxiety during the biopsy compared to women in both the active FB control group and the SC group. Additionally, women in FB and SC did not differ in the slope of their anxiety reduction during biopsy. Further, the steeper reduction in anxiety reported by GM was associated with medium effect sizes compared to the other groups (Cohen's $d > |0.4|$). These findings indicate that mindfulness-based mediation—which guides participants to bring their awareness to the present moment and observe their experience nonjudgmentally with curiosity and a sense of allowing—is an effective method for reducing anxiety during the course of a medical procedure commonly associated with high distress (Helbich et al., 1996; Lang et al., 2006). Though the present study cannot determine whether the option to participate in such an intervention may decrease anxiolytic use, similar research examining hypnosis in medical populations suggests that provision of such an intervention is likely to reduce anxiolytic use (Lang et al., 2008; Schupp et al., 2005).

It is important to point out that though the slope of anxiety ratings was steeper for those in GM compared to FB, both interventions resulted in decreased anxiety during biopsy compared to SC. This is evidenced in significant main effect of group on the last anxiety rating during biopsy, with GM and FB resulting in a mean reduction of 1.53 and 1.91 points from the first to last rating, respectively, while SC was only associated with a 0.31 reduction. Though a shift of

less than 2 points on a 10 point scale may seem small, research indicates a difference of 10-15 mm on a 100 mm Visual Analogue anxiety scale are considered clinically significant (Williams, Morlock, & Feltner, 2010).

In contrast to our hypotheses, groups did not differ in their reported anxiety ratings after the group-specific activity (i.e., after 10 minutes of guided meditation, focused breathing, or listening to NPR before the biopsy) or after the biopsy. Thus, it appears that group differences do not emerge in the absence of an acute stressor (e.g., SBB). This notion fits with experimental research indicating that brief (< 1 hour) training in mindfulness meditation reduced distress *in the face of* disturbing stimuli including CO_2 enriched air (Eifert & Heffner, 2003), painful heat (Zeidan et al., 2011), electrical shocks (Gutiérrez et al., 2004), and changing the dressing of a burn wound (Haythornthwaite et al., 2001). Intensive training and practice is likely necessary for individuals to experience reductions in anticipatory anxiety, as is seen in traditional, longer-term meditators (Lutz, McFarlin, Perlman, Salomons, & Davidson, 2013).

Mindfulness Meditation Had Little Effect on Pain and, Blood Pressure

Contrary to our hypotheses, there were no significant group differences for pain at any time during the study. Participants reported little change in pain ratings during biopsy (Figure 3), though the quadratic effect of time was significant. This is likely due to a floor effect of pain ratings, with 36% of pain ratings being 0, and only 8% of pain ratings being greater than 5. Indeed, it appears that, when pain is experimentally induced through cold or heat stimuli, brief training in mindfulness appears to increase pain tolerance and reduce the distress caused by pain (Kingston, Chadwick, Meron, & Skinner, 2007; Zeidan, Gordon, Merchant, & Goolkasian, 2010). Thus, the present intervention may have had a greater impact on pain had participants experienced greater pain.

Interestingly, there was a trend ($p = 0.09$; Cohen's d = 0.59) for women in GM to report

less post-biopsy pain (M = 1.30, SD = 1.67) compared to women in SC (M = 2.33, SD = 2.16) on a 10 point scale assessing "current pain" on the Brief Pain Inventory. Research indicates a difference of 1 point on a 10 point Visual Analogue pain scale may be clinically meaningful (Bedard et al., 2013; Kelly, 2001), suggesting that the impact of GM on post-biopsy pain may be clinically significant.

There were no group differences in SBP, DBP or pulse at any time point. Though the lack of group differences in physiological indices contradicts the findings of some studies examining the effect of brief meditation training (Campbell-Sills et al., 2006; Zeidan et al., 2010), several experimental studies did not find significant differences in physiological measures (e.g., heart rate, skin conductance; Arch & Craske, 2006; Eifert & Heffner, 2003; Erisman & Roemer, 2010). Additionally, it is important to note that though groups did not differ in VAS before or after the biopsy, groups did differ in the rate at which anxiety decreased during biopsy. Thus, there may have been group differences in physiological variables during the biopsy.

Mindfulness Meditation and Brain Activity

Results partially supported our hypothesis regarding EEG activity. Based on previous research examining changes in brain activity in novice and expert meditators, we hypothesized that, relative to FB and SC, GM would increase activity in the low frequency bands of delta, theta, and alpha (which are associated with decreased or inhibited cortical activity) in ROI associated with pain processing and emotional and cognitive engagement (S1, medial and anterior PFC, insula, and precuneus). Results indicated that GM did indeed increase delta wave activity in the left S1, left medial PFC, left insula, and bilateral precuneus compared to SC. In addition, FB also had a significant reduction in these areas relative to SC. However, contrary to hypothesis FB had the greatest delta wave activity, with more bilateral delta activity in each ROI

compared to both GM and SC. Additionally, we hypothesized that low frequency activity (i.e., delta, theta, and alpha) in each ROI would negatively correlate with self-reported anxiety and pain during biopsy. Results indicated that delta wave activity in the left medial PFC did, indeed, negatively correlate with anxiety ratings during biopsy, and delta activity in the bilateral S1, left insula, and left precuneus negatively correlated with pain ratings during biopsy. Thus, results indicated that, during biopsy, participants in FB experienced the greatest slow wave activity (potentially representing inhibition of activity) in regions associated with pain processing and emotional and cognitive engagement. Further, slow wave activity in these regions was in fact associated with reduced anxiety and pain ratings during biopsy.

Interestingly, the present study reveals a fairly consistent pattern for both GM and FB to exhibit greater delta in the *left* hemisphere compared to SC. As previously described, a considerable amount of research on EEG asymmetry indicates that greater relative left hemisphere cortical activity (represented by lower left-hemisphere alpha activity), is associated with approach-oriented emotions, while greater relative right hemisphere cortical activity (represented by lower right-hemisphere alpha activity) is associated with withdrawal-oriented emotions (Coan et al., 2006; Davidson et al., 2003). Participating in mindfulness-based interventions appears to increase left-sided asymmetry and the positive emotions associated with this asymmetry (Davidson et al., 2003; Keune et al., 2013; Moyer et al., 2011), though this shift was not always associated with self-reported improvements in affect (Moyer et al., 2011). The present study appears to contradict these findings, as greater left hemisphere delta activity (which may be indicative of lower left hemisphere cortical activity) was associated with positive self-reported outcomes of lower anxiety and pain during biopsy. To the best of our knowledge, no currently published studies have examined delta asymmetry as it relates to meditation and affect,

making it difficult to place the current asymmetrical findings for delta in context. Nonetheless, asymmetrical slow wave delta activity in the present study appears to be associated with favorable outcomes during biopsy.

Additionally, we hypothesized that GM would result in increased theta wave activity during biopsy. Results indicated that GM did, indeed, result in greater theta wave activity in the right medial and anterior PFC compared to SC. However, similar to the delta wave findings, participants in FB exhibited greater theta wave activity in the right medial PFC as well as the bilateral anterior PFC and right insula compared to SC. Unlike the delta wave findings, GM and FB did not differ in theta wave activity during biopsy for any ROI. Though we hypothesized that low frequency activity, including theta, in each ROI would negatively correlate with self-reported anxiety and pain during biopsy, theta activity was not significantly associated with anxiety or pain.

We also hypothesized that due to the brief nature of the mediation intervention, groups would not differ on high frequency bandwidth, such as beta or gamma. Results indicate that not only did groups exhibit similar beta and gamma activity during biopsy, but also similar alpha activity. The lack of group differences in the alpha bandwidth is surprising, given that differences in this bandwidth are reported fairly consistently (Fell et al., 2010). However, a review by Cahn and Polich points out that while most studies of meditators reveal a "trait" increase in alpha (i.e., increased resting state alpha following meditation training), not all studies indicate a "state" increase in alpha during meditation (Cahn & Polich, 2006). The authors of this review propose that an increase in alpha activity may be associated with relaxation, which may not be present for beginners during meditation. In the context of the present study, the lack of differences in alpha may be due to the fact that participants of GM or FB may not have been

more "relaxed" than those in SC. Rather, the delta and theta differences suggest that participants in GM and FB may have experienced greater inhibition in regions associated with cognitive and emotional processing, which in turn may have resulted in lower self-reported anxiety, though perhaps not more relaxation.

It appears that the results of the EEG activity, which indicate a more favorable neuronal response for FB participants during biopsy compared to GM and SC, do not corroborate the results of the self-reported anxiety ratings, which indicate a greater reduction in anxiety for GM during biopsy compared to FB and SC. However, it is important to note that the EEG analyses included in this study involve averaging EEG activity across time during the biopsy, whereas the main analyses of anxiety and pain reported during biopsy retains the element of time-during-biopsy. Further, the primary analysis did not indicate a significant main effect of group, but rather a significant group x time effect. Thus, the effect of group on EEG activity during biopsy is not analogous to the effect of group x time on self-reported anxiety and pain during biopsy. Future analyses of the present study's EEG data across time during the biopsy are warranted to determine whether a steeper reduction in anxiety during biopsy is associated with a steeper increase in delta wave activity in ROIs. In addition, the EEG findings need to be interpreted with caution due to the large amount of missing data.

Group Moderates the Effect of Trait Mindfulness on Anxiety and Pain

Baseline mindfulness interacted with group and time to predict anxiety ratings during biopsy. Though we hypothesized that those reporting high baseline *observing* and *nonjudgment* scores on the Five Facets of Mindfulness Questionnaire would derive the greatest benefit from GM, results indicate that several facets of mindfulness interacted with group, and not always in the expected direction. Specifically, women high in trait mindful observing and nonreaction who were

assigned to GM reported a steeper reduction in anxiety during biopsy compared to their high observing and high nonreaction counterparts assigned to FB, but, interestingly, not SC. In fact, like GM, women high in nonreaction assigned to SC also reported steeper reductions in anxiety compared to those high in nonreaction in the FB group. Thus, FB may be contraindicated for individuals with high in trait mindfulness, while GM and SC may be similarly effective at reducing anxiety for those with high trait mindfulness. Additionally, those low in mindful nonreaction experienced the greatest decrease in anxiety during biopsy if they were assigned to GM, and the same trend (though not statistically significant) can be seen for those low in mindful observing (Figure 16a). Thus, though GM and SC appear to be similarly effective at reducing anxiety during biopsy for those high in trait mindfulness, GM appears to be the best method for reducing anxiety during biopsy for those low in trait mindfulness.

Baseline mindfulness also interacted with group to predict anxiety before and pain after the biopsy. For women in SC, lower mindful nonreaction was associated with higher anxiety reported after the 10 minute pre-biopsy group specific activity. However, being in GM or FB attenuated this negative relationship, and baseline level of mindful nonreaction was unrelated to anxiety at this time point. Similarly, for women in SC, lower mindful awareness and mindful nonjudgment were associated with greater pain reported after the biopsy, but GM and FB buffered the negative effect of low mindful-awareness and mindful-nonjudgment on post-biopsy pain. Though an examination of the means based on such a small number of participants requires caution, it suggests that this was a clinically meaningful moderation effect. Women who were low in mindful nonreaction reported almost 2 points lower anxiety after the group specific activity if they were in the GM ($M = 2.6$, $SD = 1.8$) or FB ($M = 1.3$, $SD = 1.8$) groups compared to the SC group ($M = 4.5$, $SD = 6.4$). The same was true for pain reported after the biopsy.

Women low in mindful awareness who were assigned to GM (M = 0.8, SD = 1.3) or FB (M = 0.9, SD = 1.2) reported over 2 points lower post-biopsy VAS pain compared to women in SC group (M = 3.5, SD = 3.3), and women low in mindful nonjudgment who were assigned to GM (M = 2.2, SD = 4.02) or FB (M = 1.0, SD = 1.4) reported over 1.5 points lower post-biopsy pain on the VAS compared to women in SC group (M = 3.75, SD = 3.0).

A growing amount of research links trait mindfulness with lower emotional and physiological reactivity to stress (Brown, Weinstein, & Creswell, 2012; Bullis, Bøe, Asnaani, & Hofmann, 2014; van den Hurk, Janssen, Giommi, Barendregt, & Gielen, 2010). Thus, it is not surprising to see the inverse relationship between anxiety and baseline mindfulness in the SC group. Interestingly, this relationship effectively disappears for those low in mindfulness participating in the GM and FB groups. This suggests that participation in either GM or FB is particularly ideal for individuals low in trait mindfulness. While this finding contradicts that of Shapiro and colleagues, who report that individuals higher in trait mindfulness benefited more from MBSR compared to those lower in trait mindfulness (2011), it is consistent with a recent meta-analysis which found that psychosocial/behavioral treatments are most beneficial for cancer patients with pre-intervention distress (Schneider et al., 2010). Though the present study is unable to determine the mechanism of this effect, it appears that a brief mindfulness-based meditation intervention is particularly effective at reducing anxiety before and during biopsy and reducing pain after biopsy for those low in trait mindfulness.

Limitations

There are several limitations to recognize in this study. First, this study involves a relatively small sample size, particularly for moderation and EEG analyses. A larger number of evaluable EEG files would have increased the power to detect differences in brain activity associated with

group. However, it should be noted the sample size for EEG analyses in the present study (GM = 8, FB = 13, SC = 5) is similar to that of other studies utilizing brain imaging. Specifically, Allen et al.'s compared fMRI activity of 19 meditators to 19 controls (2012), Brewer and colleagues' compared fMRI activity of 12 meditators to 13 controls (2014), Lutz et al. compared fMRI activity of 14 meditators to 14 controls (2013), Tei et al. compared EEG activity of 10 meditators to 10 controls (2009), Moyer et al. compared EEG activity of 11 meditators to 10 controls (2011), Davidson and colleagues compared EEG activity of 25 meditators to 16 controls (2003), and Zeidan et al. used a within-subject design to compare fMRI activity of 15 individuals before and after meditation training (2011). Though the number of participants included in our EEG analyses may be similar to other studies, the imbalance in group size necessitates caution when interpreting the data. Specifically, though the present data suggest participants who provided evaluable EEG data did not differ on any measure from participants who did not, it cannot be ruled out that there may have been systematic differences between those who provided usable EEG data and those who did not.

Second, no autonomic measure (e.g., heart rate, blood pressure) was taken during biopsy, preventing us from determining whether groups differed on physiological measures during the acute stressor. Future research may assess autonomic activity such as heart rate using a simple, non-invasive pulse oximeter placed on participants' fingertip during biopsy.

Third, the present study does not include a measure to assess the mechanism by which GM reduced anxiety during biopsy. Models of the way in which mindfulness takes its effect highlight two possible mechanism: 1) exposure to unpleasant stimuli and 2) cognitive flexibility (i.e., the ability view one's experience objectively; Baer, 2003; Brown et al., 2007; Coffey et al., 2010; Coffey & Hartman, 2008; Hölzel et al., 2011; Shapiro et al., 2006). Due to time constraints, the

present study did not include a measure assessing these factors. Future studies can include a measure of state mindfulness, such as the Toronto Mindfulness Scale, which assesses state mindfulness using two subscales: 1) awareness of present moment experience with a quality of curiosity, and 2) accepting the present moment by taking a decentered perspective on one's present moment (Lau et al., 2006). These two subscales map onto the two mechanisms of awareness-prompted exposure and acceptance-related cognitive flexibility, and thus change in state mindfulness (i.e., from baseline to post-group-specific activity) may evaluated as a mediators of the intervention's effect.

Fourth, study staff and medical personnel were not blinded to study condition, opening the possibility that the mind-body specialist or other personnel reacted differently to participants depending on their group. Future research in which the intervention is delivered automatically (e.g., through audio recording delivered via ear-bud to the participant) may overcome the possible bias associated with unblinded study and medical staff. Additionally, blinded staff could provide valuable third-party data about the biopsy. For example, after the biopsy is complete, nurses and technologists blinded to study condition could complete a brief (< 1 minute) survey on how smoothly they believe the procedure went, and how cooperative the patient was during the procedure. However, it is important to note that, unlike the vast majority of studies examining mind-body interventions, the participants in the present study were blinded to the purpose of the study (i.e., examining the benefits of meditation), decreasing the effects of bias due to knowing group assignment. In fact, we are aware of only one other published study of a mind-body intervention that has used this patient blinding strategy (Wang et al., 2010). Finally, the majority of participants were white, non-Hispanic, married and highly educated. Thus, future research is needed to test the generalizability of these findings to more diverse populations.

Future Research

In addition to the improvements for future research described above, several changes to the design of the present study design may improve cost effectiveness and reduce barriers to implementing GM into the standard of care during an invasive medical procedure. First, the current study required two study personnel to be present during the biopsy procedure. The cost associated with such additional personnel is a significant obstacle to implementing a nonpharmacological intervention, such as GM, into SBB standard of care. Thus, future research could eliminate the need for a research assistant to collect self-reported anxiety ratings during biopsy by having participants hold a ball equipped with a pressure-sensor capable of continuously recording the amount of pressure applied to the ball. Participants could squeeze the ball according to the level of anxiety they felt, thus provide an automated, continuous measure of anxiety throughout the procedure. The "ComfyBall," a nonverbal pain communication tool fitting this description, was recently proposed at the 2013 MIT Innovations in Health Care Conference, and could be a valuable tool for improving patient reporting and cost savings (Shah et al., 2014).

Additionally, a live mind-body specialist could be replaced by audio-guided GM. Evidence suggests that the benefits of non-pharmacologic interventions are not contingent upon live delivery. Research published as early as 1970 indicated no difference in the effect of one hour of live compared to recorded hypnosis or progressive muscle relaxation on self-reported anxiety, heart rate, or respiratory rate in a sample of undergraduate women (Paul & Trimble). Further, Kwekkeboom and colleagues (2008) found audio-recorded progressive muscle relaxation to reduce cancer-related pain in hospitalized patients. Finally, a meta-analysis of 20 studies examining the beneficial effects of hypnosis compared to standard care for surgical

patients indicated no difference between effect sizes associated with live versus recorded delivery methods (Montgomery et al., 2002). Delivering GM through audio recording would have the added benefit of enabling study and medical staff to be blinded to study condition.

A second way to improve cost effectiveness may be to screen individuals prior to enrolling them in a larger-scale study of GM. The moderation analyses in the present study indicated that, while individuals high in trait mindfulness fair similarly in the GM and SC groups, individuals low in trait mindfulness derived the greatest benefit from being in the GM group. Thus, in keeping with the recent recommendations against an "all comers" approach to nonpharmacological interventions, it may be prudent to include only individuals likely to benefit from such an intervention (Coyne, Lepore, & Palmer, 2006; Schneider et al., 2010). Further research should explore other possible moderators of the benefits of GM such as baseline anxiety. It makes theoretical sense that GM, or even FB, would be more helpful for those high in pre-biopsy anxiety, however, that questions needs to be answered.

Summary

The present study had five specific aims. A summary of the results for each of these aims are presented below. First, results suggest that a brief guided mindfulness meditation (GM) while women are undergoing SBB is acceptable and feasible. It is likely that, without the inclusion of EEG acquisition, acceptability would be even higher. Second, results suggest that participation in a mindfulness-based meditation is associated with steeper reduction in anxiety during the biopsy compared to participation in focused breathing or standard care, though no differences in anxiety were noted immediately before or after the procedure. Third, participating in a mindfulness meditation was not associated with significant differences in pain, heart rate, or blood pressure before, during, or after the study compared to participating in focused breathing

or standard care. However, there was a trend, which approached clinical significance, for participation in mindfulness-based meditation to be associated with lower post-biopsy pain. Fourth, compared to GM and SC, FB appears to have resulted in the greatest neuronal quieting (potentially related to inhibition) in regions associated with pain processing, emotional and cognitive engagement. Importantly, the EEG analyses are preliminary and involve comparing neuronal activity averaged across time during biopsy, rather than examining the change in neuronal activity during biopsy. Thus, the effect of group on EEG activity during biopsy cannot be mapped on to the effect of the group-by-time interaction on self-reported anxiety during biopsy. Fifth, results suggest that participating in brief mindfulness-based meditation is particularly effective at reducing anxiety before and during biopsy and reducing pain after biopsy for those low in trait mindfulness.

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Table 1. Medical and Demographic Data

	GM (n = 30)		FB (n = 30)		SC (n = 16)	
	No.	%	No.	%	No.	%
Age (M, SD)	55.13	12.41	55.1	10.38	55.94	11.02
Hispanic/Latina Ethnicity	5	19.23	5	17.86	5	18.75
Race						
Asian/Pacific Islander	1	3.45	2	6.67	1	6.25
Black/African American	2	6.9	3	10	3	18.75
White/Caucasian	22	75.86	22	73.33	12	75
Other	4	13.79	3	10	0	0
Married/Partnered	20	68.97	19	63.33	12	75
College Degree or Higher	20	66.66	15	50	7	43.75
Income > $75,000	17	56.67	15	49.97	8	50
Full time Employment	16	55.17	13	43.33	9	56.25
Post-Menopausal	19	63.33	21	70	13	81.25
BIRADS*						
0	2	6.67	2	6.67	1	6.25
I-III	2	6.66	2	6.67	0	0
IV	21	70	22	73.33	12	75
V-VI	4	13.34	3	10	2	12.5
Unknown	1	3.33	1	3.33	1	6.25
Anxiety Medication	4	13.33	4	13.33	3	18.75
Previous Cancer Diagnosis	9	30	11	36.67	7	43.75
Previous SBB	7	23.33	5	16.67	3	18.75
Cores Obtained (M,SD)	8	2.96	8	2.96	7	1.99

**Note:* BIRADS (Breast Imaging Reporting and Data System) is a rating system used by medical professionals to communicate risk of breast cancer based on mammography results. A rating of 0 indicates an incomplete mammogram; 1-3 indicate negative or benign findings; 4 indicates suspicious abnormality; 5 indicates mammography is highly suggestive of malignancy; 6 indicates known carcinoma. *Abbreviations*: SBB = Stereotactic Breast Biopsy.

Table 2. Raw Group Means

	GM (n=30)		FB (n=30)		SC (n=16)		
Measure (Range)	*M*	*SD*	*M*	*SD*	*M*	*SD*	*p-value*
VAS Anxiety (0-10)							
Baseline	2.96	2.69	3.33	2.67	2.56	2.99	0.51
Post-Group Activity	1.87	1.98	1.73	2.03	1.50	2.34	0.92
First Rating During Biopsy	3.50	2.69	3.48	3.27	3.56	3.08	0.69
Last Rating During Biopsy	1.97[a]	2.14	1.57[a]	1.92	3.25[b]	3.09	*0.01*
Post-Biopsy	1.18	1.76	1.04	1.67	1.56	2.10	0.26
VAS Pain (0-10)							
Baseline	0.86	1.65	1.07	1.55	0.94	1.53	1.00
Post-Group Activity	0.67	1.42	0.83	1.46	0.56	1.03	0.70
First Rating During Biopsy	1.50	1.87	1.66	1.90	1.50	1.63	0.66
Last Rating During Biopsy	1.93	2.05	1.80	1.99	2.31	2.75	0.42
Post-Biopsy	1.29	2.24	0.86	1.11	1.13	2.13	0.61
STAI - State (20-80)							
Baseline	40.96	10.56	40.85	11.94	40.25	13.47	0.94
Post-Group Activity	30.93	8.76	30.41	10.06	31.09	13.78	0.86
Post-Biopsy	32.17	10.69	31.09	9.85	34.90	12.44	0.41
BPI Pain (No. with pain)							
Baseline (n, %)	9	31.03	8	29.63	9	60.00	0.16
Post-Biopsy (n, %)	13	54.17	18	66.67	7	46.67	0.42
BPI Pain Average (0-10)							
Baseline	1.55	2.05	1.81	1.98	1.73	1.71	0.99
Post-Biopsy	1.30	1.73	1.89	1.80	2.33	2.16	0.09
BPI Interference (0-10)							
Baseline	0.95	1.46	1.02	1.62	1.31	2.02	0.65
Post-Biopsy	1.26	1.67	1.04	1.30	1.54	2.28	0.91
Systolic Blood Pressure							
Baseline	127.52	18.24	129.97	14.94	129.46	14.69	0.65
Post-Group Activity	127.13	16.86	133.54	16.55	127.79	14.20	0.32
Post-Biopsy	71.75	20.36	71.75	17.13	135.29	16.40	0.17
Diastolic Blood Pressure							
Baseline	77.17	11.42	77.10	10.30	76.54	9.58	0.98
Post-Group Activity	75.00	10.71	78.16	10.10	76.14	10.35	0.17
Post-Biopsy	70.69	11.80	70.47	8.34	80.33	11.73	0.51
Pulse							
Baseline	71.75	12.52	71.75	11.62	76.98	14.85	0.39
Post-Group Activity	70.69	10.40	81.55	11.65	75.08	15.57	0.73
Post-Biopsy	75.74	13.71	74.81	9.48	74.55	16.57	0.11

Table 3. VAS Anxiety and Pain reports during biopsy

	Group*Time Interaction		**GM vs. SC**			**FB vs. SC**			**GM vs. FB**		
	$F_{(2, 220)}$	*p*-value	β (SE)	d*	*p*-value	β (SE)	d	*p*-value	β (SE)	d	*p*-value
Change in Anxiety	7.94	<0.001	-0.107 (0.032)	-0.448	<0.001	-0.014 (0.031)	-0.062	0.65	-0.093 (0.026)	-0.475	<0.001
Change in Pain	0.11	0.89	-0.018 (0.038)	-0.064	0.63	-0.012 (0.036)	-0.046	0.73	-0.06 (0.031)	-0.026	0.85

Note: Values based on mixed linear multilevel models covarying for the respective baseline VAS ratings and ethnicity.

*Cohen's d

Table 4. Pairwise Comparisons of Delta Activity in ROIs during Biopsy

		GM vs. SCs					FB vs. SC					GM vs. FB				
ROI	Hem.	*t*-value	*p*-value	X	Y	Z	*t*-value	*p*-value	X	Y	Z	*t*-value	*p*-value	X	Y	Z
S1	R	NS	> 0.2	-	-	-	3.90	0.001	10	-36	66	-3.21	0.004	35	-31	61
BA 3	L	2.86	0.014	-45	-22	38	4.49	<0.001	-30	-32	48	-2.33	0.030	-10	-36	66
mPFC	R	NS	> 0.2	-	-	-	2.67	0.016	25	50	34	NS	> 0.2	-	-	-
BA 9	L	2.22	0.046	-50	7	37	3.09	0.007	-45	7	37	-2.22	0.038	-25	45	35
aPFC	R	NS	> 0.2	-	-	-	2.55	0.021	20	59	20	-2.08	0.051	45	48	-7
BA 10	L	NS	> 0.2	-	-	-	2.22	0.040	-20	59	20	-2.49	0.022	-25	54	20
Insula	R	NS	> 0.2	-	-	-	2.52	0.022	30	-33	20	-2.92	0.009	40	-43	21
BA 13	L	3.02	0.011	-54	-38	20	5.08	<0.001	-54	-38	20	-2.63	0.016	-40	-43	21
Precuneus	R	2.37	0.035	20	-51	44	5.26	<0.001	20	-51	44	-3.84	0.001	20	-62	31
BA 7	L	2.53	0.026	-30	-46	53	4.27	<0.001	-25	-46	44	-3.24	0.004	-5	-75	45

Abbreviations: ROI = region of interest; Hem = hemisphere; BA = Brodmann area; S1 = primary somatosensory cortex; mPFC = medial prefrontal cortex; aPFC = anterior prefrontal cortex; NS = not significant; X, Y, and Z represent Talairach coordinates.

Table 5. Correlation of Delta Activity in ROIs with Anxiety and Pain Ratings during Biopsy

		Anxiety Correlation					Pain Correlation				
ROI	Hem.	Pearson's *r*	*p*-value	X	Y	Z	Pearson's *r*	*p*-value	X	Y	Z
S1	R	NS	> 0.2	-	-	-	**-0.415**	0.031	45	-16	61
BA 3	L	-0.370	0.058	-50	-12	41	**-0.492**	0.009	-30	-31	57
mPFC	R	-0.309	0.117	5	31	31	-0.321	0.103	45	7	37
BA 9	L	**-0.412**	0.033	-35	7	37	-0.300	0.128	-40	12	36
aPFC	R	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
BA 10	L	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
Insula	R	NS	> 0.2	35	1	18	-0.285	0.150	30	-28	20
BA 13	L	-0.346	0.077	-35	1	18	**-0.389**	0.045	-30	-38	20
Precuneus	R	0.342	0.081	35	-6	49	-0.371	0.057	5	-32	43
BA 7	L	0.306	0.12	-10	-75	50	**-0.441**	0.021	-30	-46	53

Note: Correlations significant at the $p < 0.05$ are listed in bold. *Abbreviations*: ROI = region of interest; Hem = hemisphere; BA = Brodmann area; S1 = primary somatosensory cortex; mPFC = medial prefrontal cortex; aPFC = anterior prefrontal cortex; NS = not significant; X, Y, and Z represent Talairach coordinates.

Table 6. Pairwise Comparisons of Theta Activity in ROIs during Biopsy

Theta		**GM vs. SC**					**FB vs. SC**					**GM vs. FB**				
ROI	Hem.	*t*-value	*p*-value	X	Y	Z	*t*-value	*p*-value	X	Y	Z	*t*-value	*p*-value	X	Y	Z
S1	R	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
BA 3	L	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
mPFC	R	2.27	0.042	30	35	26	2.92	0.010	35	31	31	NS	> 0.2	-	-	-
BA 9	L	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
aPFC	R	2.74	0.018	25	53	-11	2.92	0.010	25	53	-11	NS	> 0.2	-	-	-
BA 10	L	NS	> 0.2	-	-	-	2.08	0.053	-10	38	-10	NS	> 0.2	-	-	-
Insula	R	2.08	0.060	30	24	-1	2.72	0.015	30	24	-1	NS	> 0.2	-	-	-
BA 13	L	NS	> 0.2	-	-	-	2.02	0.059	-45	9	-5	NS	> 0.2	-	-	-
Precuneus	R	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
BA 7	L	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-

Abbreviations: ROI = region of interest; Hem = hemisphere; BA = Brodmann area; S1 = primary somatosensory cortex; mPFC = medial prefrontal cortex; aPFC = anterior prefrontal cortex; NS = not significant; X, Y, and Z represent Talairach coordinates.

Table 7. Correlation of Theta Activity in ROIs with Anxiety and Pain Ratings during Biopsy

Theta		**Anxiety Correlation**					**Pain Correlation**				
ROI	Hem.	Pearson's *r*	*p*-value	X	Y	Z	Pearson's *r*	*p*-value	X	Y	Z
S1	R	0.358	0.067	20	-36	57	NS	> 0.2	-	-	-
BA 3	L	0.347	0.076	-25	-32	48	NS	> 0.2	-	-	-
mPFC	R	-0.279	0.159	50	31	31	NS	> 0.2	-	-	-
BA 9	L	0.378	0.052	-45	16	36	NS	> 0.2	-	-	-
aPFC	R	-0.283	0.153	45	44	12	NS	> 0.2	-	-	-
BA 10	L	NS	> 0.2	-	-	-	NS	> 0.2	-	-	-
Insula	R	0.266	0.180	35	-38	20	NS	> 0.2	-	-	-
BA 13	L	0.350	0.074	-20	38	20	NS	> 0.2	-	-	-
Precuneus	R	**0.472**	0.013	20	-71	40	NS	> 0.2	-	-	-
BA 7	L	**0.429**	0.026	-5	-62	31	NS	> 0.2	-	-	-

Note: Correlations significant at the $p < 0.05$ are listed in bold. *Abbreviations*: ROI = region of interest; Hem = hemisphere; BA = Brodmann area; S1 = primary somatosensory cortex; mPFC = medial prefrontal cortex; aPFC = anterior prefrontal cortex; NS = not significant; X, Y, and Z represent Talairach coordinates.

Figure 1. Consort diagram

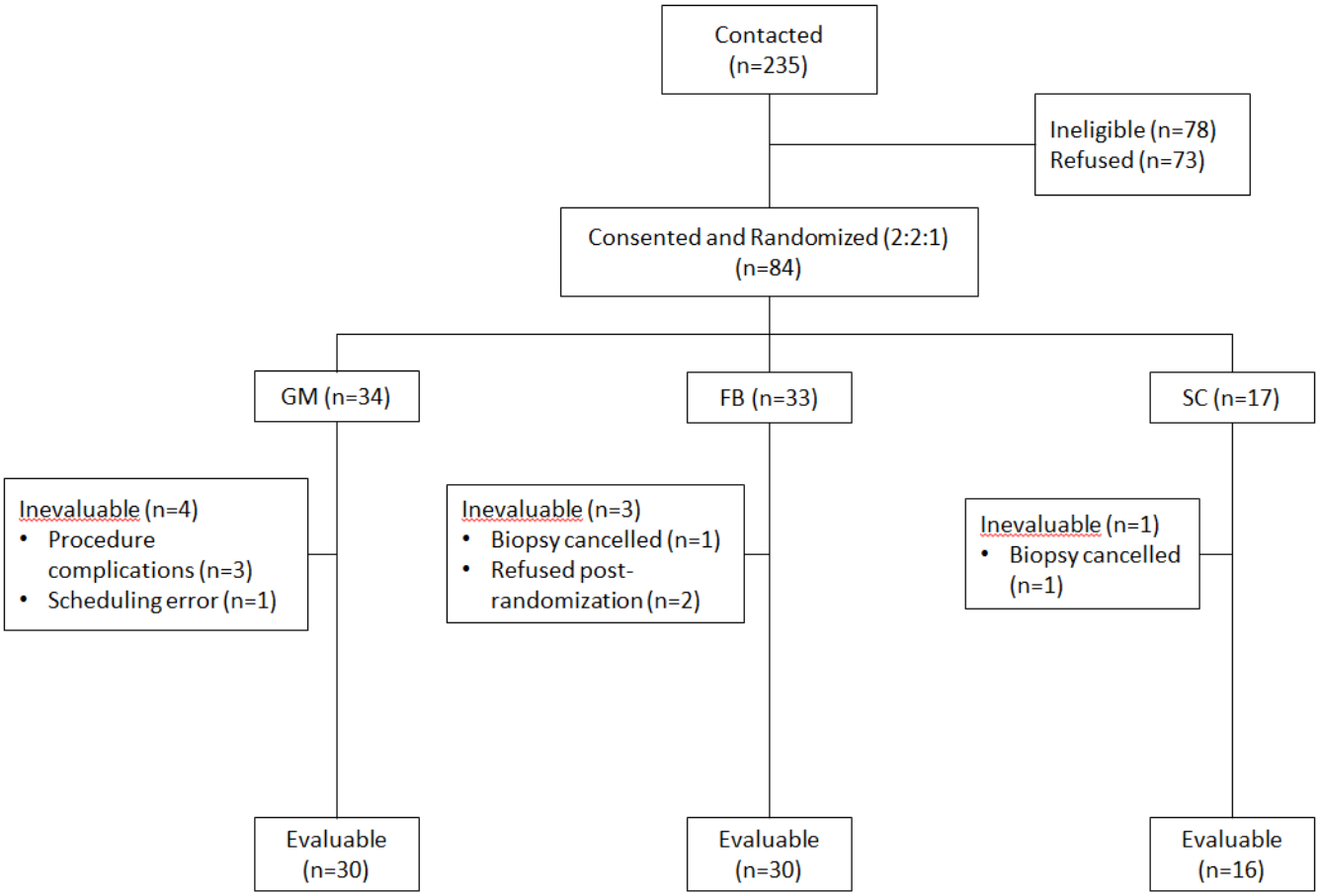
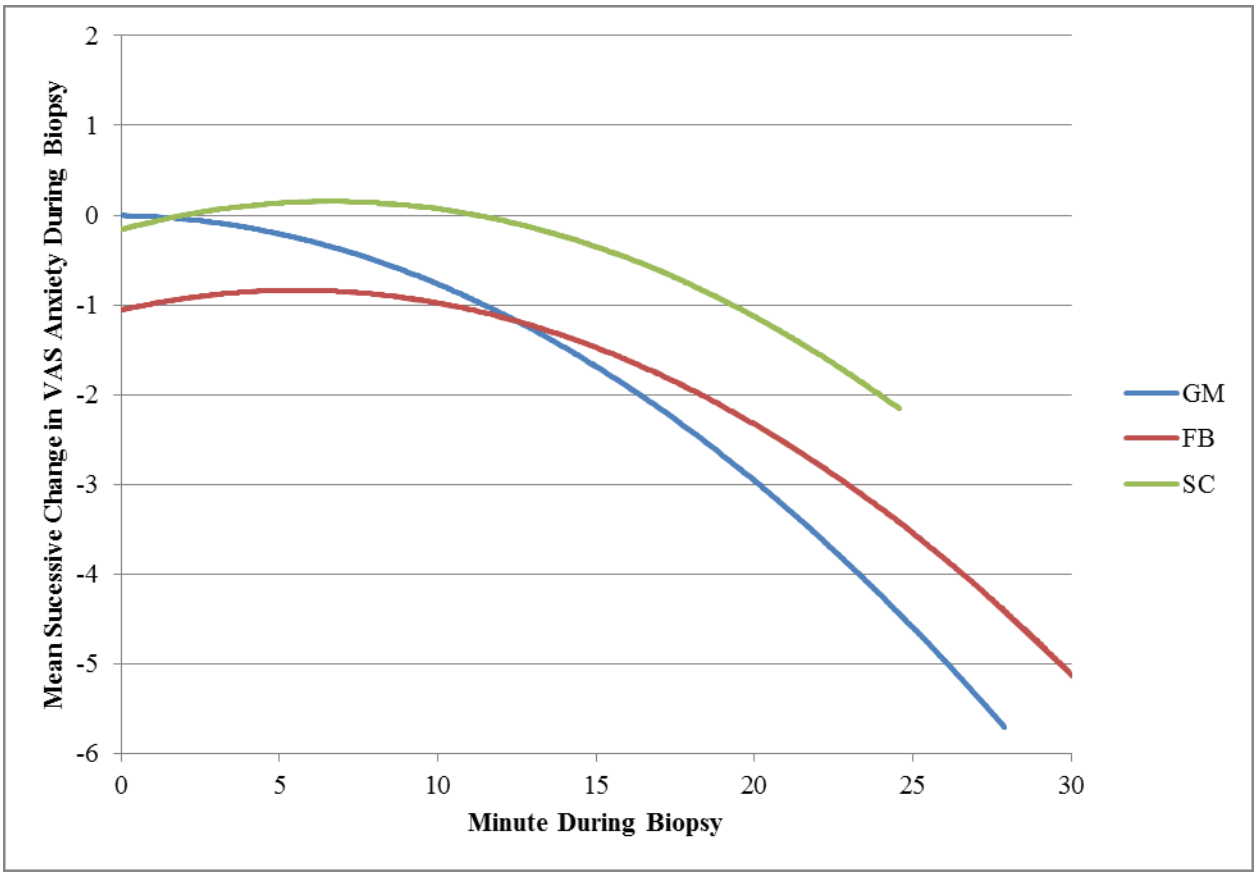
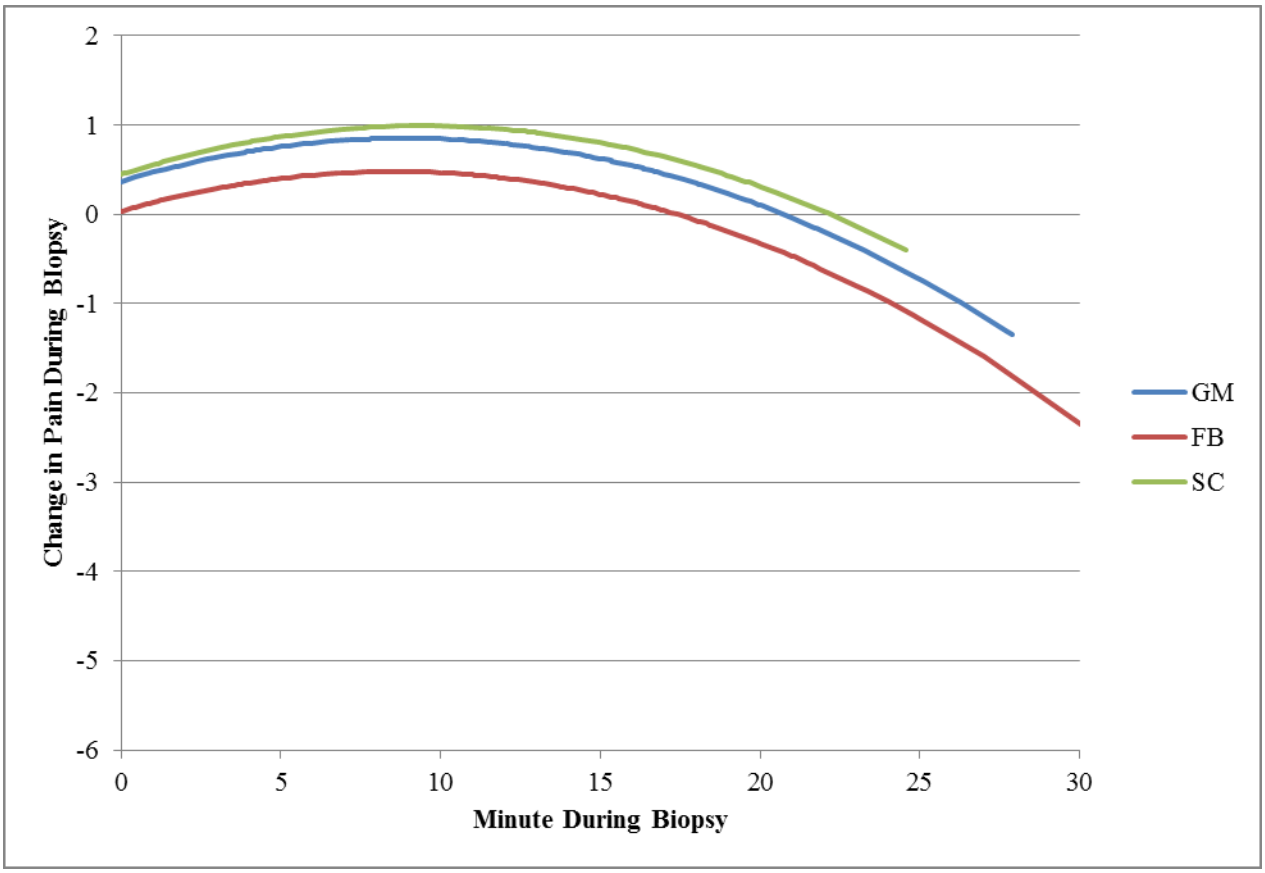


Figure 2. Quadratic estimate of change in VAS anxiety during biopsy



Note: Figure represents mixed linear multilevel model examining the effects of group, time, and group by time interaction effects on change in VAS anxiety ratings from the first rating of the biopsy during the procedure, covarying for baseline VAS anxiety and ethnicity, with time during biopsy a quadratic term in the model. Women in GM reported a steeper reduction in anxiety during the biopsy compared to FB and SC (p's = 0.001), while FB and SC reported similar reductions in anxiety during biopsy (p = 0.65). *Abbreviation*: VAS = Verbal Assessment Scale.

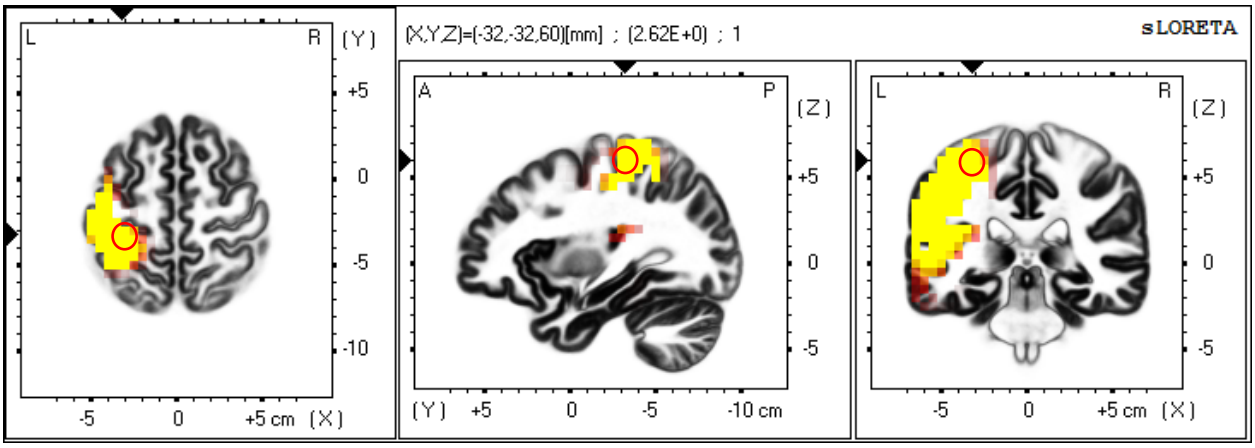
Figure 3. Quadratic estimate of change in VAS pain during biopsy



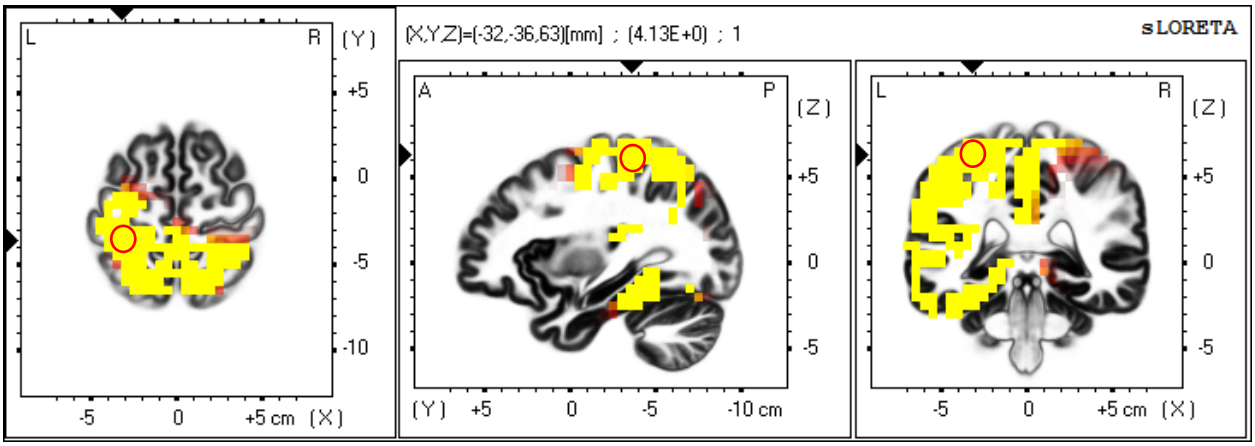
Note: Figure represents mixed linear multilevel model examining the effects of group, time, and group by time interaction effects on change in VAS pain ratings from the first rating of the biopsy during the procedure, covarying for baseline VAS pain and ethnicity, with time during biopsy a quadratic term in the model. The slope of pain over time during biopsy did not differ by group ($p = 0.89$). *Abbreviation*: VAS = Verbal Assessment Scale.

Figure 4. Pairwise comparisons of delta activity in the left S1 (BA 3)

4a. GM > SC, $p = 0.014$



4b. FB > SC, $p < 0.001$



4c. GM > FB, $p = 0.030$

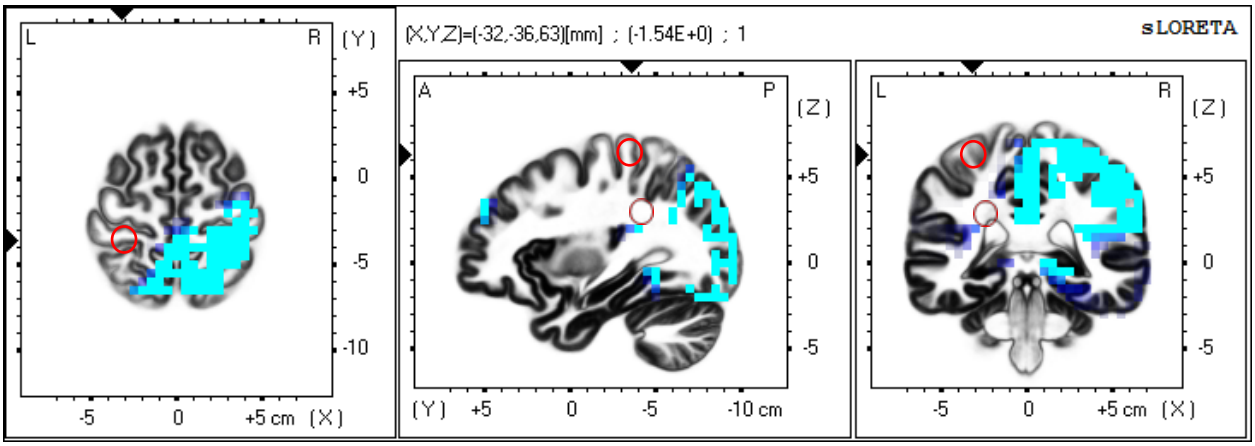
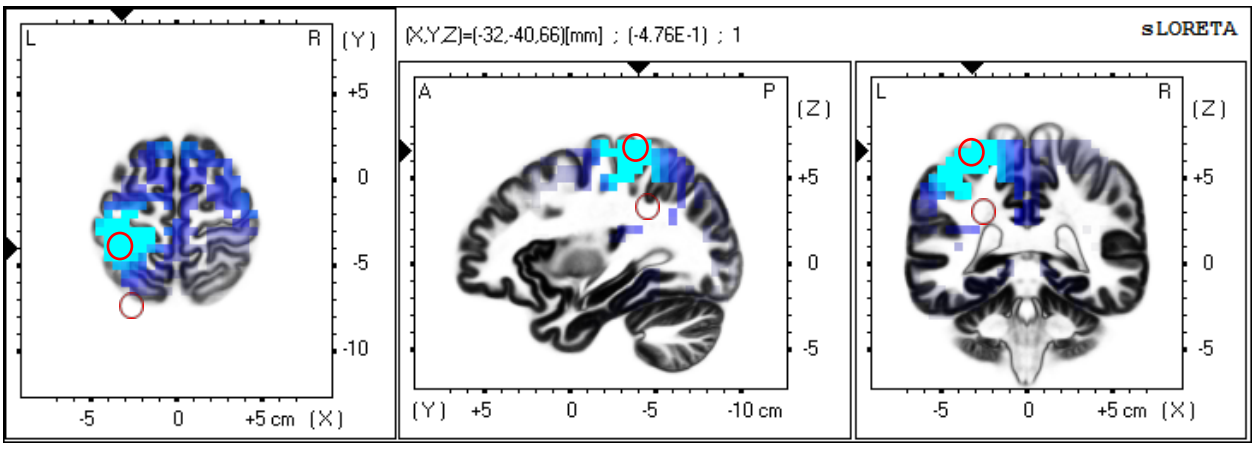


Figure 5. Correlation of delta activity in the left S1 with pain ratings during biopsy

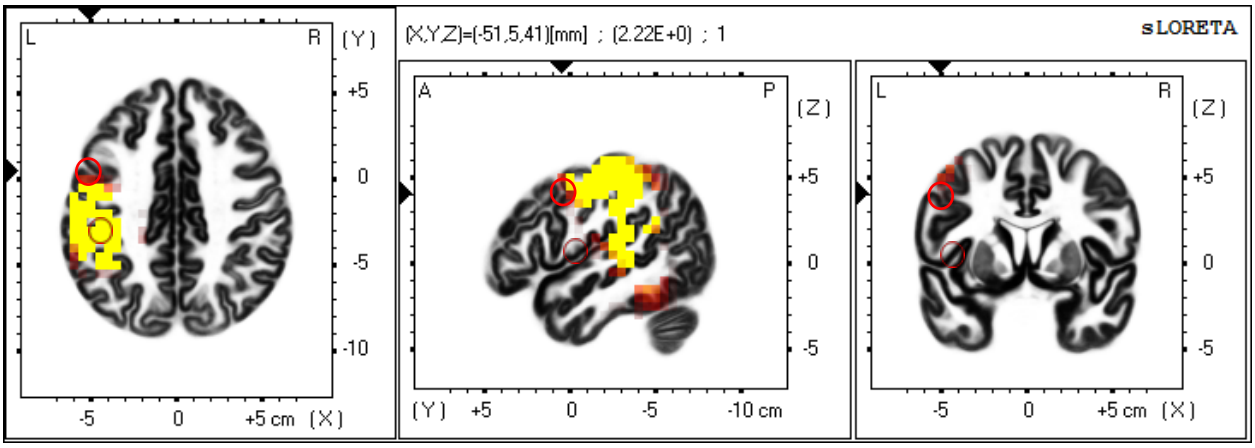


Note: Delta activity in the S1 during biopsy negatively correlated with pain ratings ($p = 0.009$).

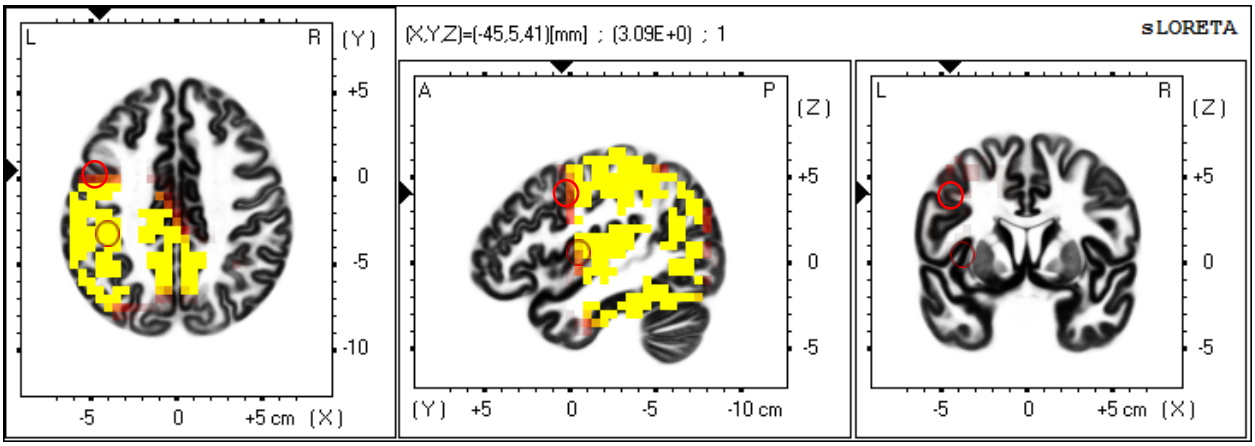
Abbreviations: S1 = primary somatosensory cortex

Figure 6. Pairwise comparisons of delta activity in the left medial PFC (BA 9)

6a. GM > SC, p = 0.046



6b. FB > SC, p = 0.007



6c. GM > FB, p = 0.038

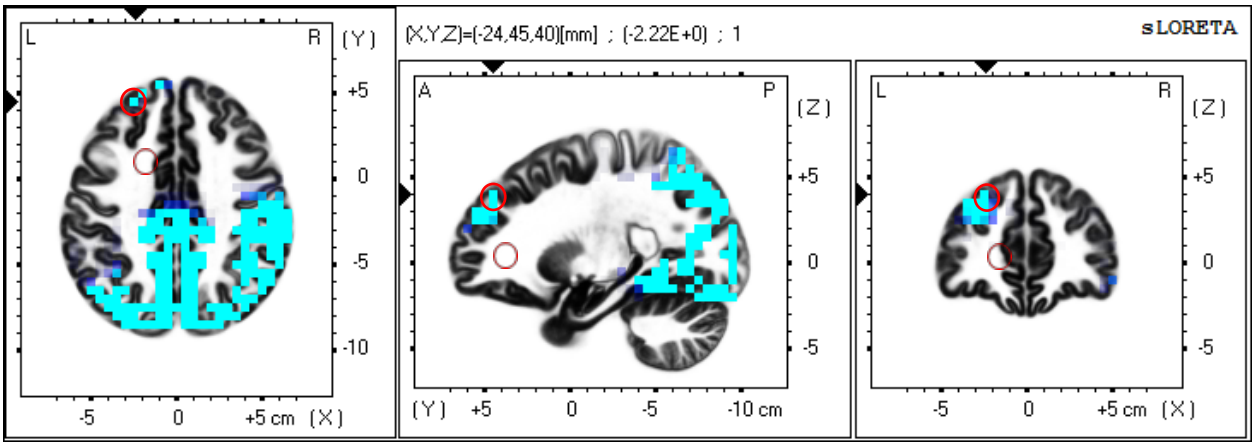
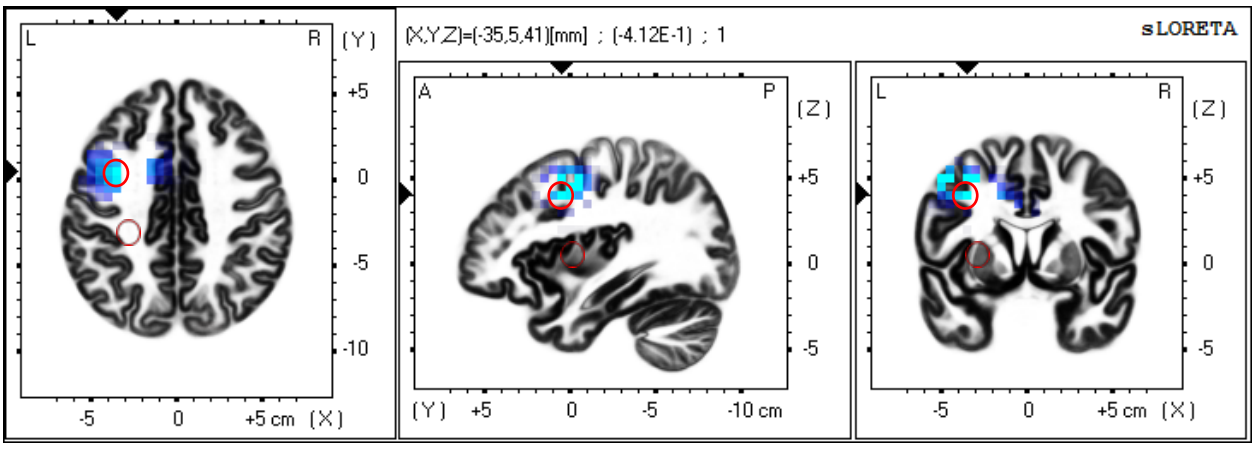


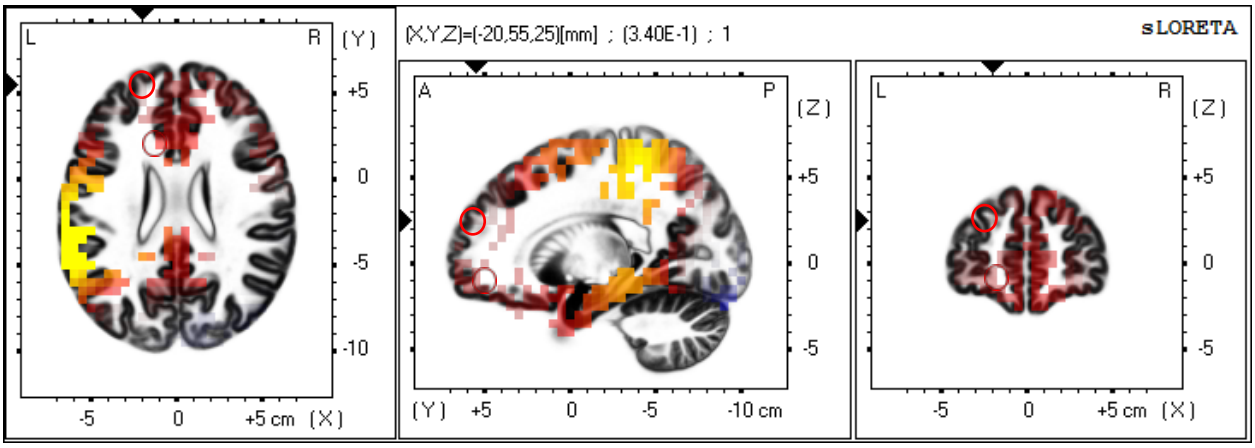
Figure 7. Correlation of delta activity in the left medial PFC with anxiety ratings during biopsy



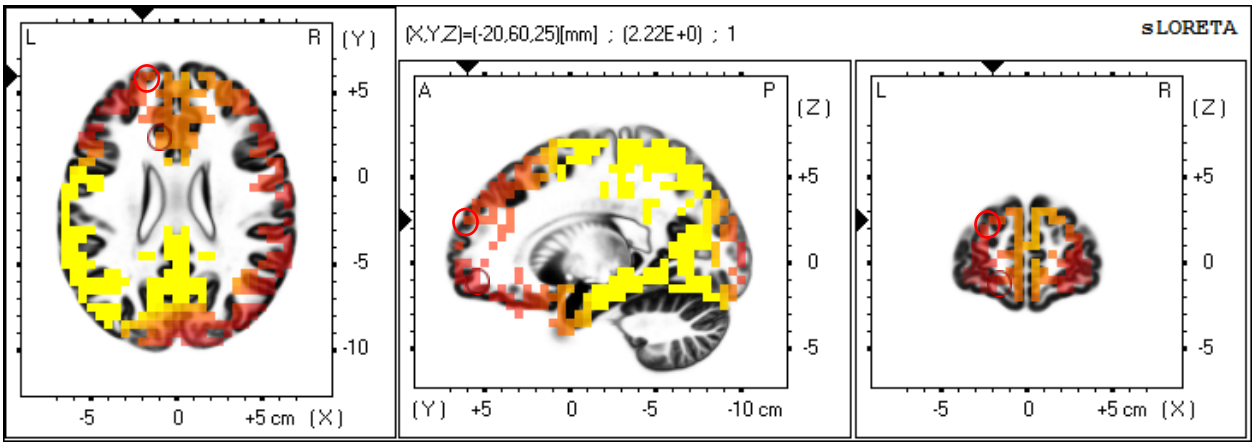
Note: Delta activity in the left medial PFC during biopsy negatively correlated with anxiety ratings ($p = 0.003$). *Abbreviations*: PFC = prefrontal cortex

Figure 8. Pairwise comparisons of delta activity in the left anterior PFC (BA 10)

8a. GM > SC, p > 0.2



8b. FB > SC, p = 0.040



8c. GM > FB, p = 0.022

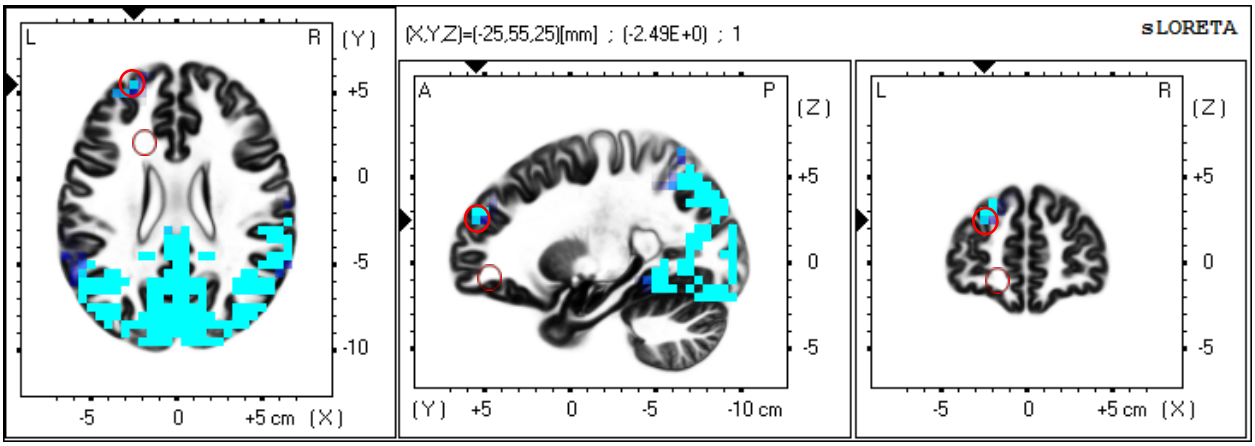
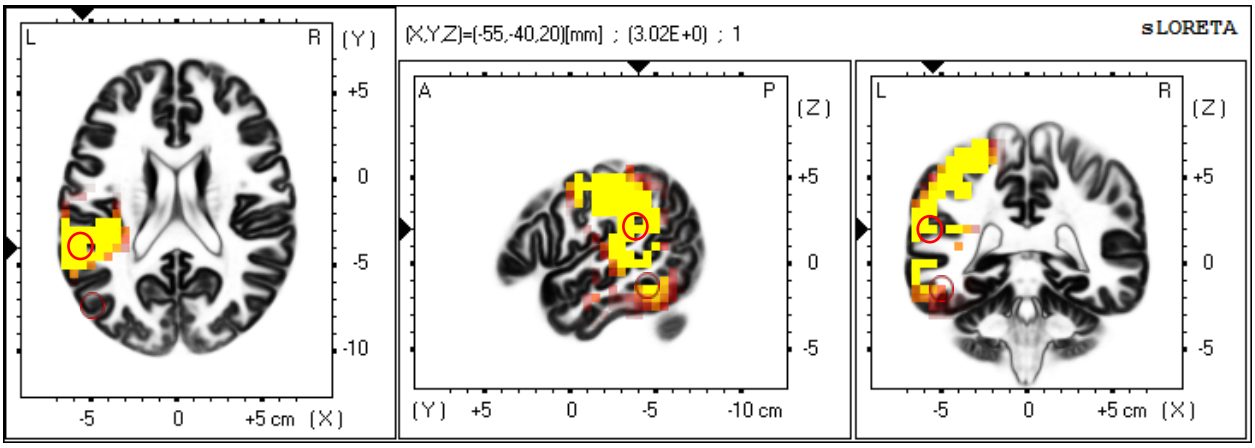
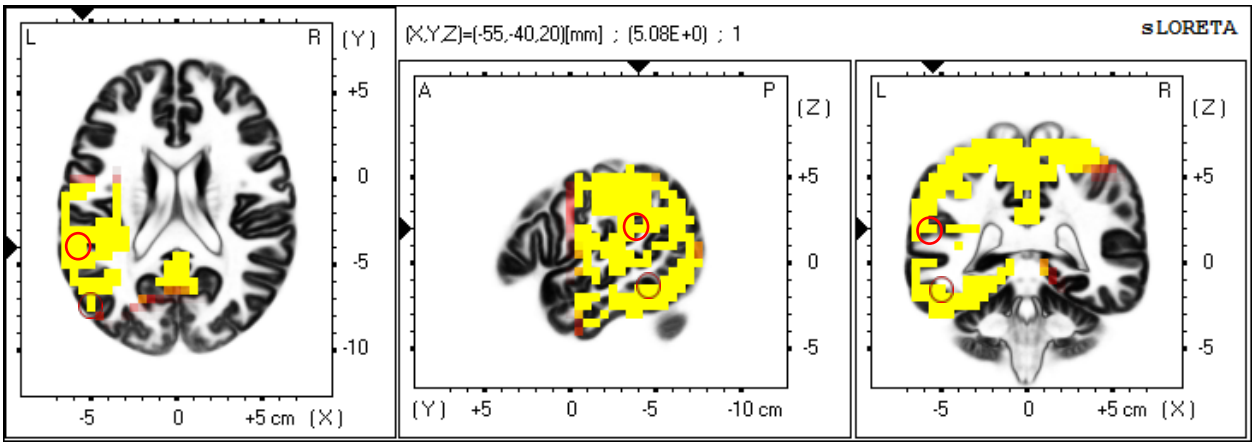


Figure 9. Pairwise comparisons of delta Activity in the left insula (BA 13)

9a. GM > SC, p = 0.011



9b. FB > SC, p < 0.001



9c. GM > FB, p = 0.016

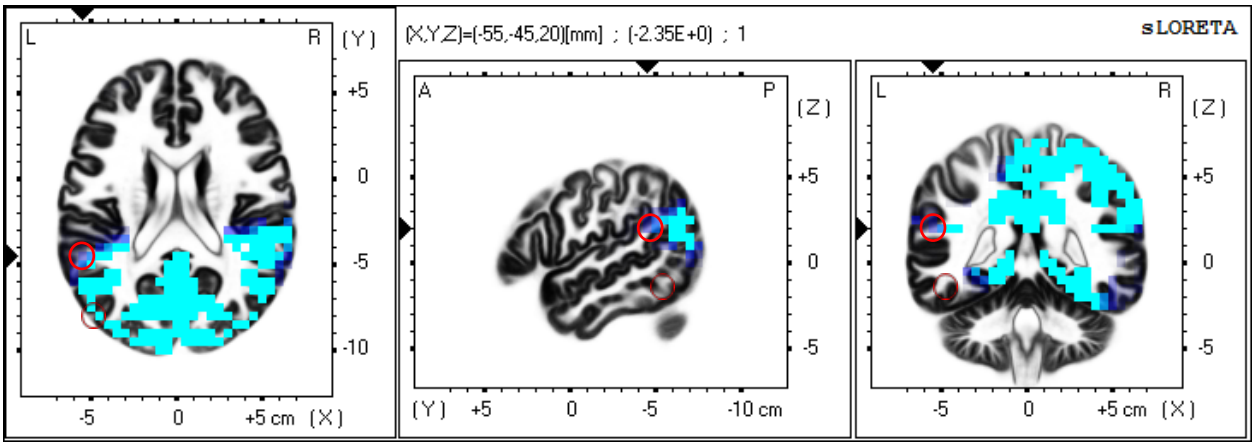
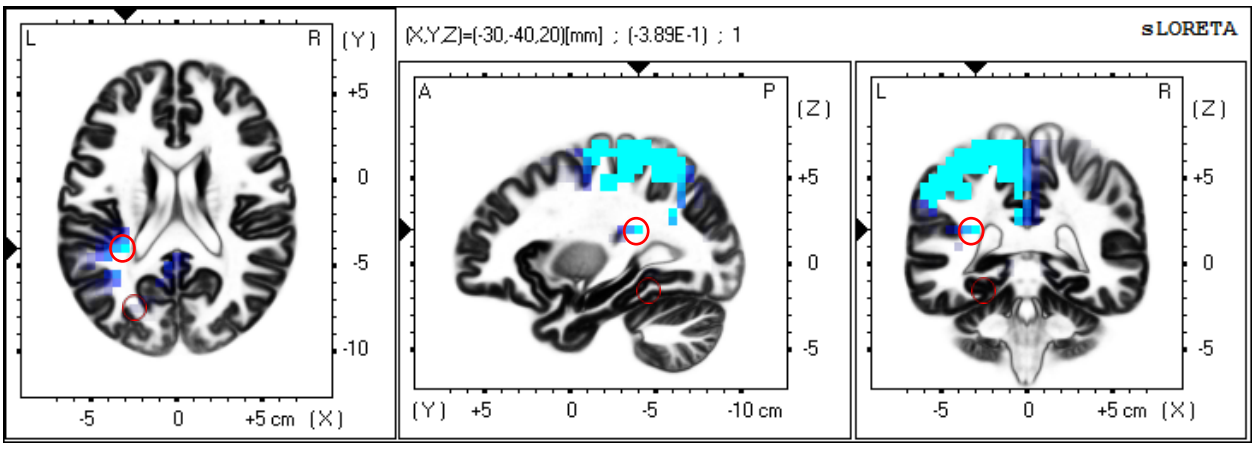


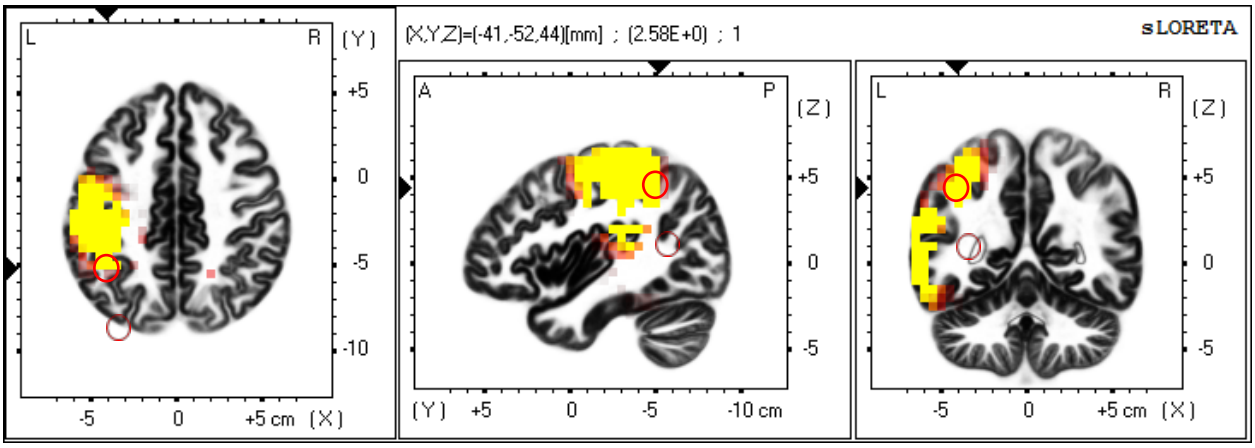
Figure 10. Correlation of delta activity in the left insula with pain ratings during biopsy



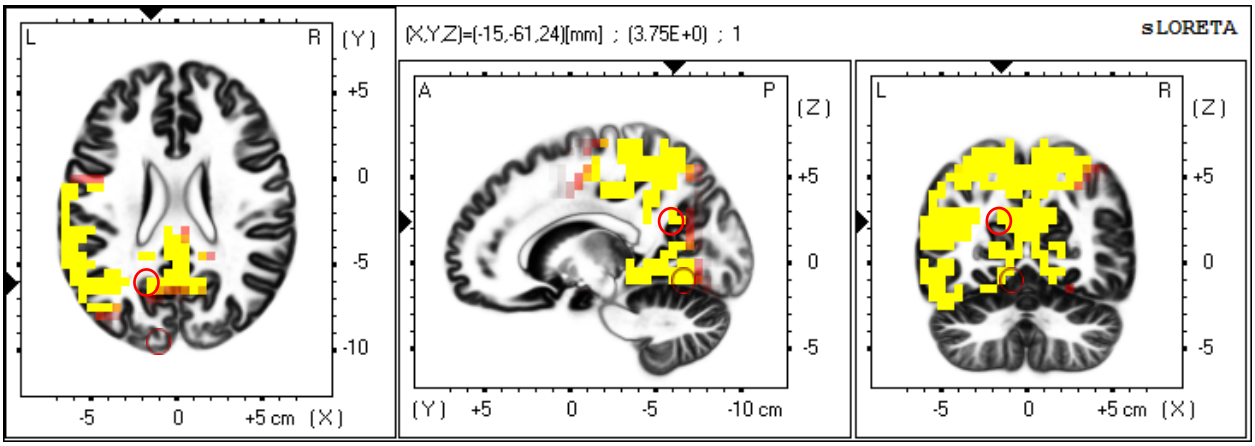
Note: Delta activity in the left insula during biopsy negatively correlated with pain ratings (p = 0.045).

Figure 11. Pairwise comparisons of delta activity in the left precuneus (BA 7)

11a. GM > SC, p = 0.026



11b. FB > SC, p < 0.001



11c. GM > FB, p = 0.004

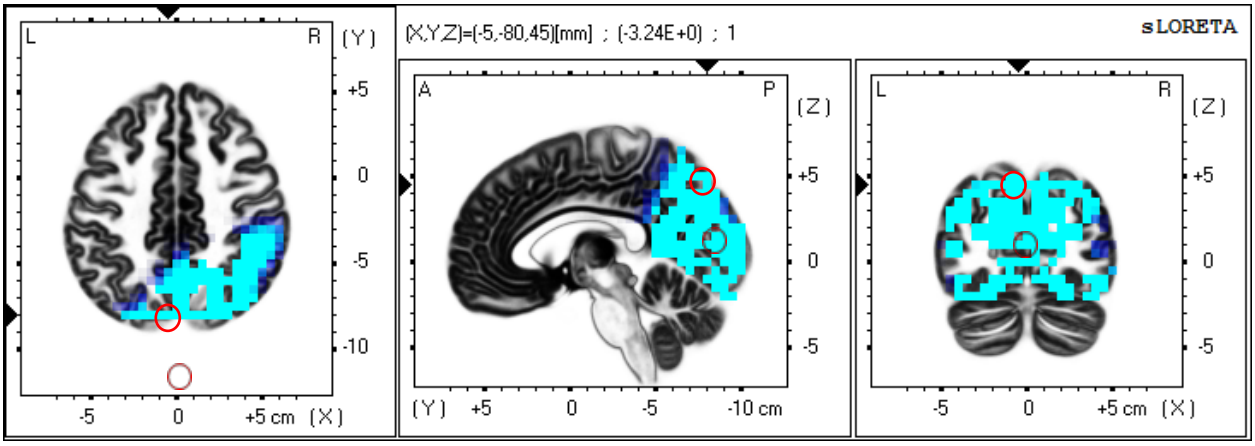
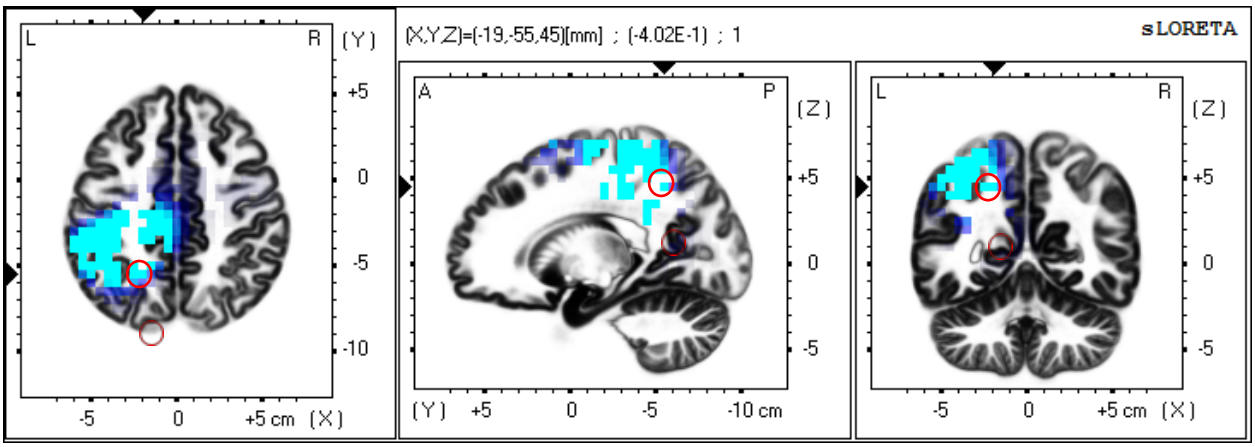


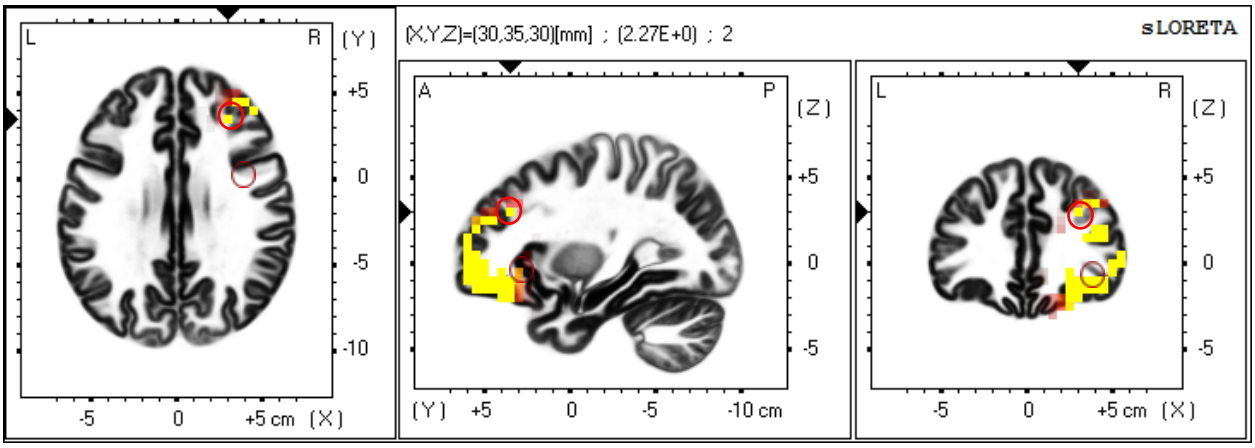
Figure 12. Correlation of delta activity in the left precuneus with pain ratings during biopsy



Note: Delta activity in the left precuneus during biopsy negatively correlated with pain ratings (p = 0.021).

Figure 13. Pairwise comparisons of theta activity in the right medial PFC (BA 9)

13a. GM > SC, p = 0.042



13b. FB > SC, p = 0.010

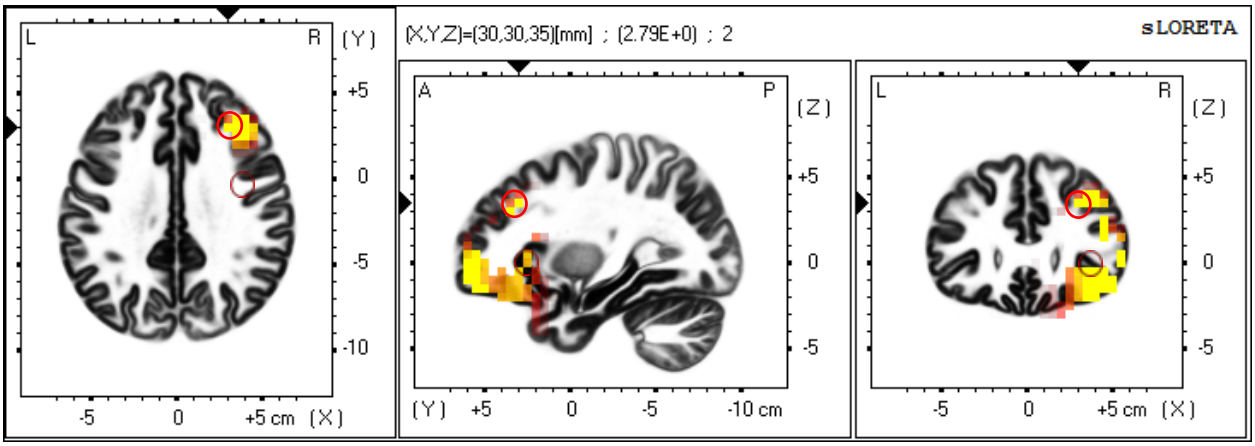
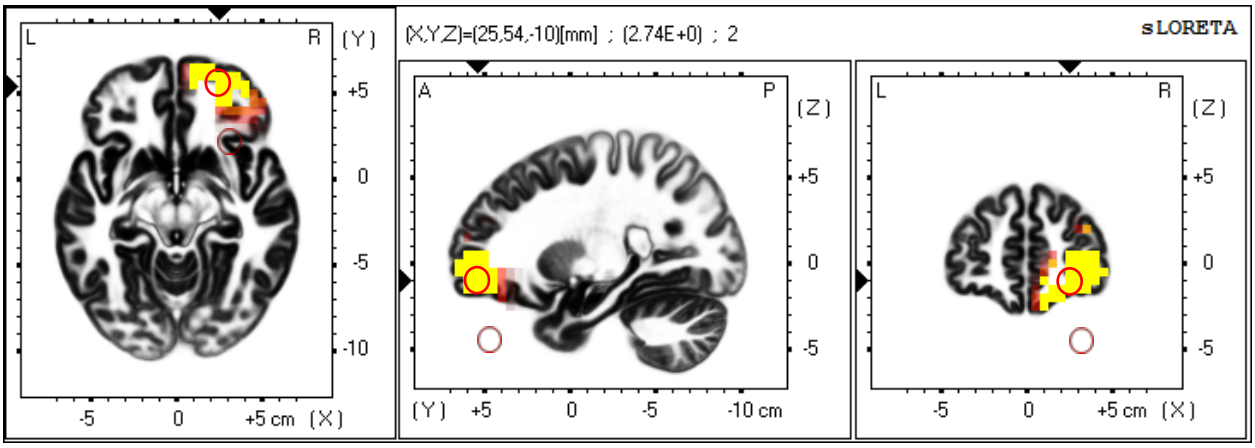


Figure 14. Pairwise comparisons of theta activity in the right anterior PFC (BA 10)

14a. GM > SC, p = 0.018



14b. FB > SC, p = 0.010

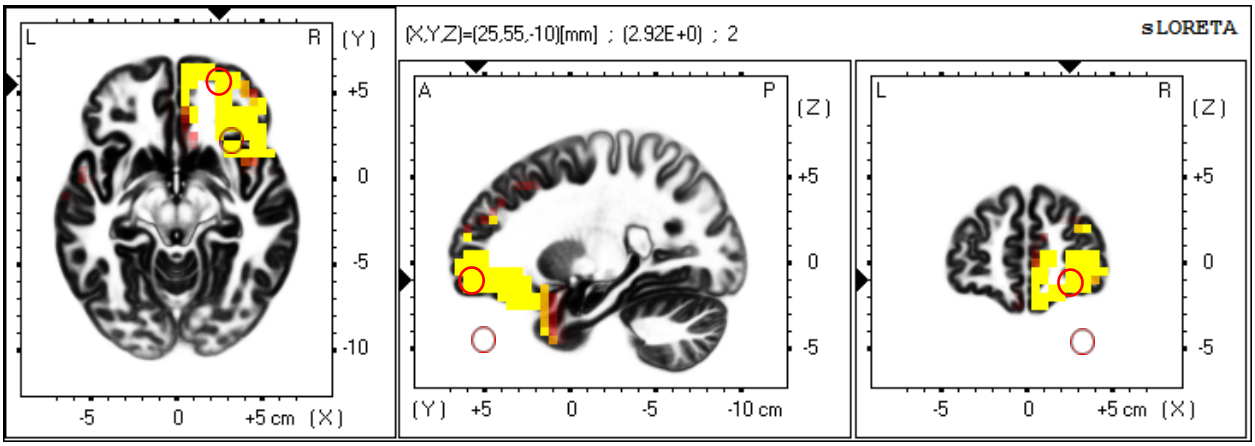
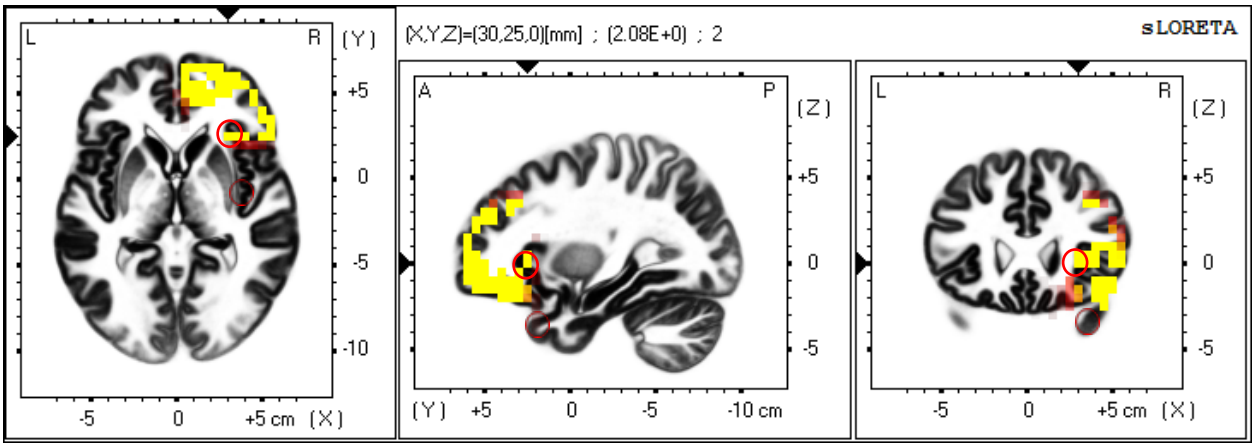


Figure 15. Pairwise comparisons of theta activity in the right insula (BA 13)

15a. GM > SC, p = 0.060



15b. FB > SC, p = 0.015

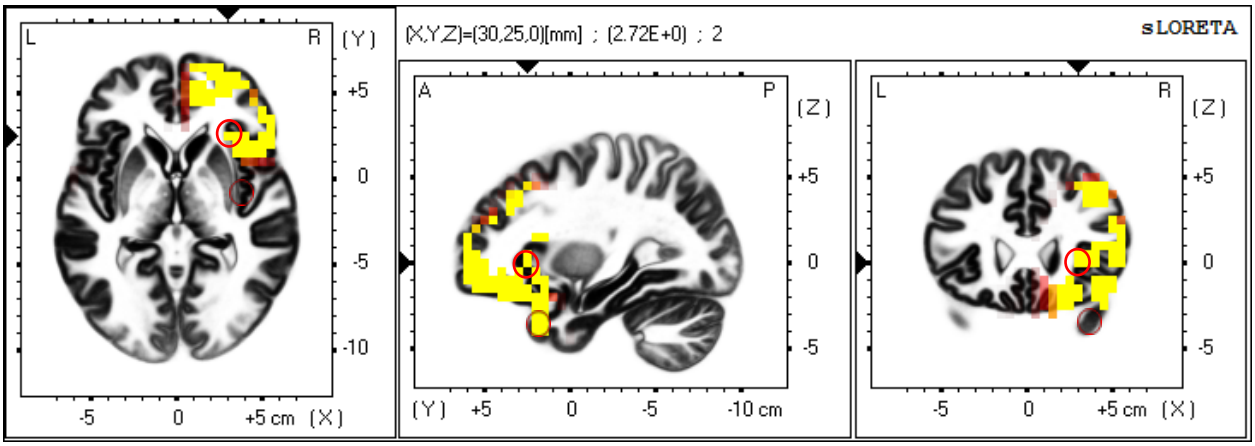
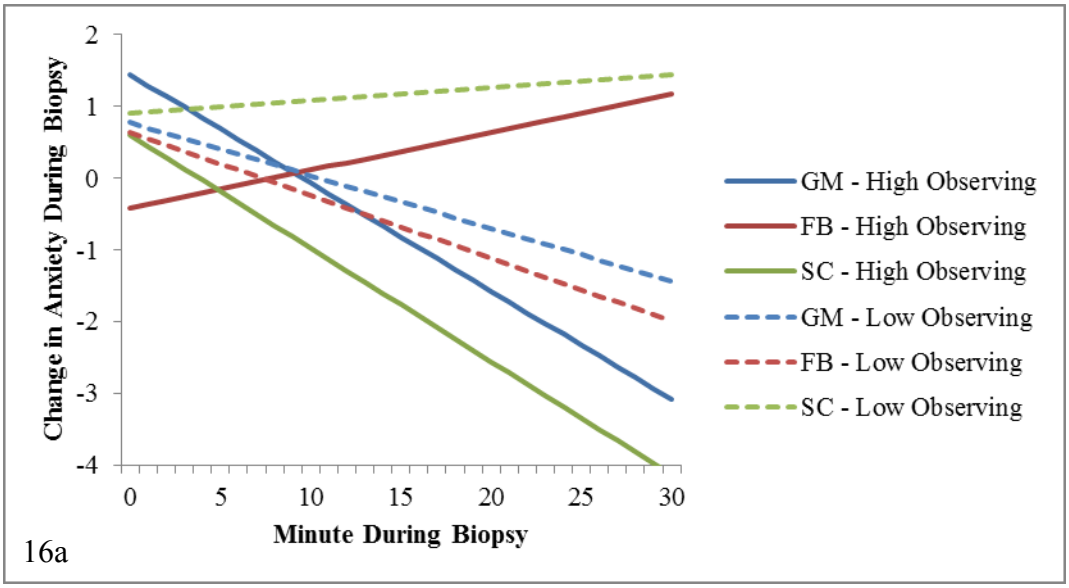
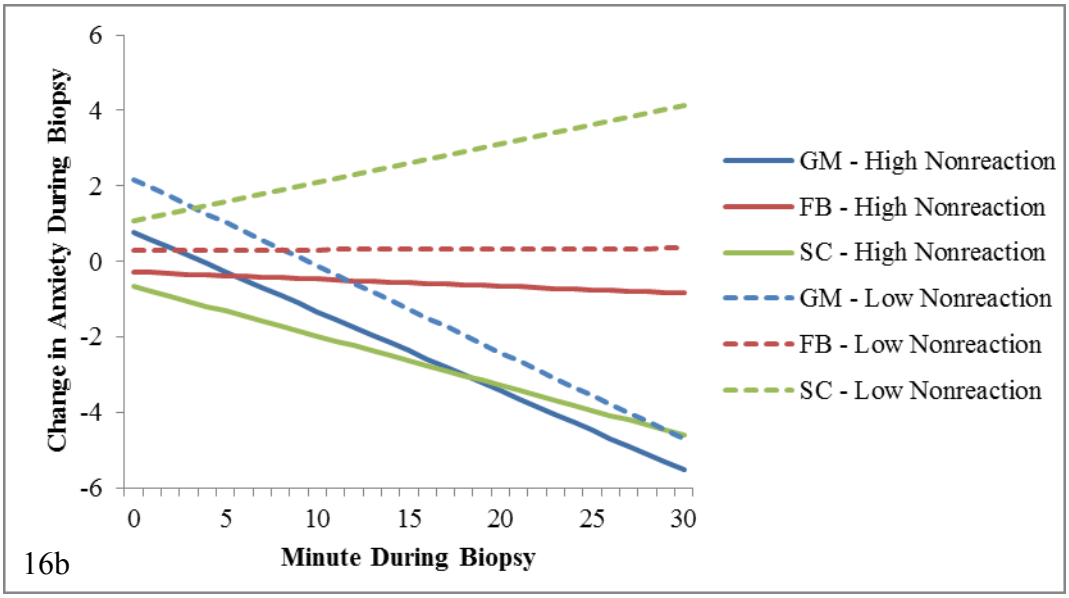


Figure 16. Group moderates the effect of trait mindfulness on anxiety during biopsy

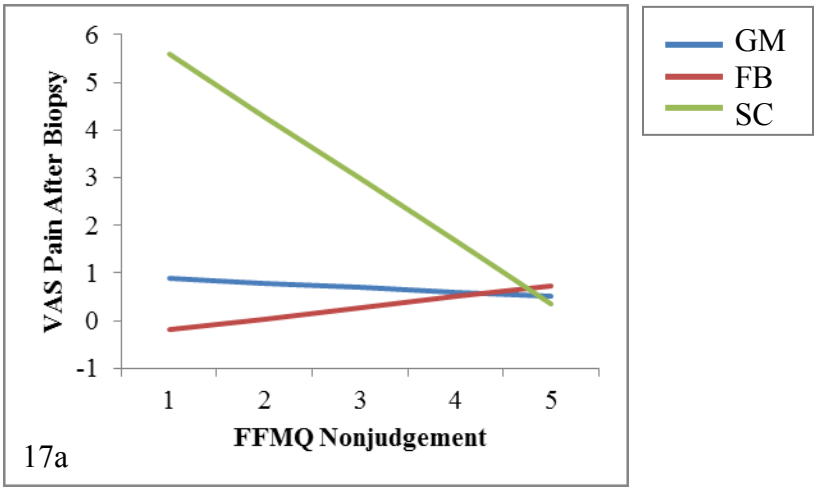


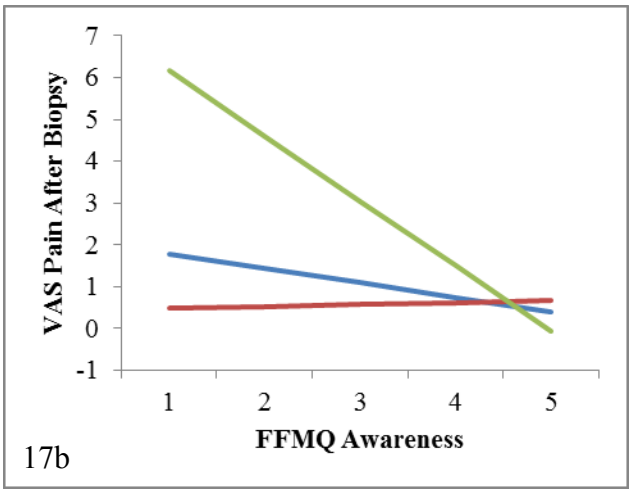


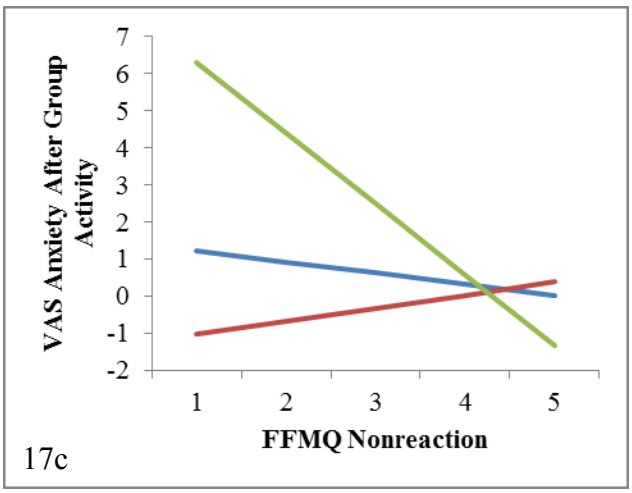
Note: Women with high observing scores in GM reported a steeper reduction in anxiety compared to those in FB (p = 0.01), but not SC. Women with high observing scores in FB and SC did not differ in anxiety reduction. Women with low observing scores did not differ by group in their reduction in anxiety. Women with high nonreaction scores in GM and SC reported a steeper reduction in anxiety compared to those in FB (p = 0.001), but not SC. Women with high nonreaction scores in SC reported a steeper reduction in anxiety compared to those in FB (p =

0.05). Women with low nonreaction scores in GM also reported a steeper reduction in anxiety compared to those in FB ($p = 0.005$), and a trend toward a steeper reduction in anxiety compared to SC ($p = 0.1$). Women with low nonreaction scores in FB and SC did not significantly differ in anxiety reduction.

Figure 17. Group moderates the effect of trait mindfulness on anxiety before and pain after biopsy







Note: Compared to SC, GM and FB buffered the negative association between anxiety during biopsy and mindful nonjudgment, awareness, and nonreaction (p's ≤ 0.05).