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Novel measurements for radiodermatitis research and clinical care: A pilot and feasibility study☆

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ABSTRACT

Purpose: The role of clinician-measured breast length and bra cup size in the development of radiodermatitis over time and the efficacy of using multiple measurements of skin toxicity during radiotherapy were piloted. The feasibility of measures to be used in a larger future study was assessed.
Methods and materials: Participants included women receiving normofractionated or accelerated external breast radiotherapy provided in the supine position using 3-dimensional conformal techniques at a US community cancer center. Acute skin toxicity was assessed using the RTOG scale in 7 areas within the treatment field across 6 timepoints. The total score for the 7 areas was calculated each week. Breast length was measured, examined as an acute radiodermatitis risk factor, and compared against reported bra cup size. RM-ANOVAs examined radiodermatitis using maximum skin toxicity and 7 sites in the radiotherapy field over 6 timepoints. Correlation was implemented to explore the relationship between study variables.
Results: Forty women consented to this study. Increase in breast length significantly correlated with increase in maximum RTOG score ($p = .04$); increased RTOG score in the upper medial breast quadrant ($p = .04$), upper lateral quadrant ($p = .02$), lower lateral quadrant ($p = .02$), inframammary fold ($p = .001$); with increasing BMI ($p = .002$) and bra cup size ($p = .0003$). The clinician-measured breast lengths and participant-reported bra cup sizes were discordant. Participants completed all measures and measurements including breast length.
Conclusions: Our results suggest that measuring breast length and assessing radiodermatitis in multiple areas of the treatment field is feasible. These measures may increase the sensitivity of skin toxicity assessment.

1. Introduction

Previous studies of radiodermatitis are limited in that they were typically conducted at major medical centers in urban areas. Additional studies are needed in community settings. Predictors consistently associated with radiodermatitis development over the past two decades of research include breast characteristics, body mass index, smoking, and skin phototype.

The purpose of this study was to examine the feasibility and pilot a collection of measures planned for use in a larger future study and provide a scientific estimate of the sample size needed for the future study. Our goals were to assess (1) the feasibility of eligibility and exclusion criteria, recruitment, retention, refusal, and adherence; (2) explore the role of clinician-measured breast length and participant-reported bra cup size in the development of radiodermatitis over time on treatment and the efficacy of using multiple measurements of skin toxicity in the treatment field, and (3) calculate effect sizes needed to estimate required sample sizes for future studies.

1.1. Breast characteristics

Large breasts are consistently associated with increased risk of radiodermatitis (De Langhe et al., 2014; Porock et al., 1998). However, few studies of radiodermatitis have included breast measurements such as asymmetry and ptosis as variables. Most pairs of breasts are naturally asymmetrical; conversely, bra cups are equal in size implying bra size may not be an optimal metric as a predictor for radiodermatitis. Liu et al. (2010). used medical imaging to calculate seven unique

Abbreviations: BMI, Body mass index; BSAF, Breast skin assessment form; DF, Degrees of freedom; Inframam fold, Inframammary fold; M, Mean; n, number of participants assessed; η2, eta squared; PI, Principal investigator; RM-ANOVA, Repeated measures analysis of variance; RT, Radiotherapy; RTOG, Radiation Therapy Oncology Group; SD, Standard deviation

☆ Laura Beamer was a PhD student at the University of Utah while the work was done, but graduated in 2016.

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measurements of the breasts (i.e., nipple level, nipple to midline distance, inferior mammary fold level, breast width, breast projection, breast volume, and anterior chest wall projection) in 100 Chinese women. They found that 100% of the women had at least one of the seven parameters differ significantly between the breast pairs (Liu et al., 2010). Wood et al. (2008) found 80% of their study population wore incorrectly fitting bras. Moreover, bra cup size may not identify the amount of breast ptosis (i.e., drooping). Pendulous breasts increase the surface area in the inframammary fold and may cause a bolus effect during radiotherapy and predispose the woman to radiodermatitis (Barrett-Lennard and Thurstan, 2008). These issues support the need for a more precise measurement of the breast in research studies when breast size is used to predict an outcome such as radiodermatitis. Clinician-measured breast length may provide an answer to this need.

Hidvegi et al. (2004) measured the torso surface area of 40 healthy women to estimate body surface area in burn victims and found "for every increase in cup size, the surface area of a woman's anterior trunk increased by a factor of 0.1 relative to her posterior trunk area" (p. 1595). Additionally, these researchers found the pectoral region may account for almost 10% of the total body surface area when the bra cup size is greater than or equal to DD (Hidvegi et al., 2004).

1.2. Skin toxicity

Although there are several scales used to measure radiodermatitis, one global assessment of skin in the treatment field is used to identify the maximum level of toxicity. However, the current standard of using a single assessment does not adequately quantify the body surface area impacted by radiodermatitis. Moreover, there is a precedent for making multiple assessments of skin toxicity (De Langhe et al., 2014; Hindley et al., 2014).

1.3. Body mass index (BMI)

Overweight (BMI > 25) and obesity (BMI > 30) are related to increased incidence of breast cancer (American Cancer Society, 2018; Centers for Disease Control & Prevention [CDC]; De Langhe et al., 2014; Liu et al., 2008; Porock et al., 1998). However, they are also known risk factors for the development of radiodermatitis (Méry et al., 2015; Pommier et al., 2004).

1.4. Smoking

A strong association exists between smoking during radiotherapy and the development of radiodermatitis (De Langhe et al., 2014; Porock et al., 1998; Sharp et al., 2011). Similarly, Fisher et al. (2000) found a history of lifelong tobacco *abstinence* was associated with a reduction ($p = .026$) of radiodermatitis development. Smoking tobacco causes vasoconstriction of the cutaneous vasculature (Monfrecola et al., 1998). This tobacco-induced vasoconstriction was scientifically measured using thermography, laser doppler flowmetry, plethysmography, videomicroscopy, pulse oximetry, and oxygen electrode (Hindley et al., 2014).

1.5. Skin phototype

Fitzpatrick devised a system describing skin types according to risk of developing sunburn (Astner and Anderson, 2004). The system implements six phototypes that range from "do not tan, burn easily" to "become darker, do not burn" (Wolff and Johnson, 2009). Ironically, skin that is darkly pigmented and does not burn but becomes darker is the phototype that often suffers the most severe radiodermatitis (Yamazaki et al., 2012). These findings suggest the need for additional studies to explore the use of skin phototype instead of race and ethnicity as a potential predictor of radiodermatitis development.

1.6. Nonphysical sequelae of radiodermatitis

The nonphysical sequelae of radiodermatitis include treatment delays, early termination of treatment, suffering, and lost contributions to the family and society. Bese et al. (2007) found a significant difference ($p = .022$) in the five and ten-year locoregional control of breast cancer recurrence in favor of women with treatment interruptions of 0–7 as compared to > 8 days.

2. Materials and methods

This article presents a portion of a mixed-methods study that also examined skin-related and global quality of life in the presence of radiodermatitis (Beamer and Grant, 2018; Beamer and Grant, 2019). The first author served as the study principal investigator (PI) and single rater of measures and outcomes. Each participant served as her own control for the outcomes in this study using repeated measurements.

2.1. Setting

The study was completed at a Comprehensive Community Cancer Program in northwestern Illinois, USA. The external treatments were delivered via a Varian Clinac EX linear accelerator using 3-dimensional conformal techniques including stand open field, hard and enhanced dynamic wedges, and irregular surface compensation. All the patients were treated in the supine position. Thirty-three women received normofractionated (i.e., 180–200 cGy) doses and seven women received accelerated treatment using fractions of 266 cGy.

2.2. Feasibility measurement

A feasibility study looks at individual components of a scientific investigation and is used to build the foundation of a larger future study (Tickle-Degnen, 2013). On the other hand, a pilot study is the miniature version of a larger future study (Arain et al., 2010). Thabane et al. (2010) table on reasons for conducting pilot studies provided a framework for assessing the feasibility of our study. The four domains framing our assessment included process, management, resources, and scientific.

2.3. Pilot measurements

2.3.1. Biometrics

Height and weight were measured at baseline, then the BMI was calculated using the online Centers for Disease Control and Prevention Adult BMI Calculator (CDC). Participant-reported bra cup and band size was recorded. The PI measured the length of the affected breast in women who underwent lumpectomy or mastectomy with immediate reconstruction. The contralateral breast was measured in women who underwent mastectomy without reconstruction. The measurement was standardized by using the midclavicular line as a landmark, then measuring the breast length from inframammary fold to nipple and areola or surgical incision line in centimeters using a 182.88 cm disposable paper measuring tape manufactured by Medline with the patient positioned in high Fowler's position.

2.3.2. Maximum skin toxicity

Maximum grade of skin toxicity in the radiation treatment field was assessed weekly by the PI using the RTOG Acute Radiation Morbidity Scoring Criteria for skin. Developed by radiation oncology experts for use in clinical trials with an acute radiodermatitis outcome, the RTOG scale includes four ordinal grades of radiation-induced skin toxicity including "0" no change from baseline; "1" follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating; "2" tender or bright erythema, patchy moist desquamation/moderate edema; "3"

Participant ID_____

Date_____

Cumulative radiation dose _____

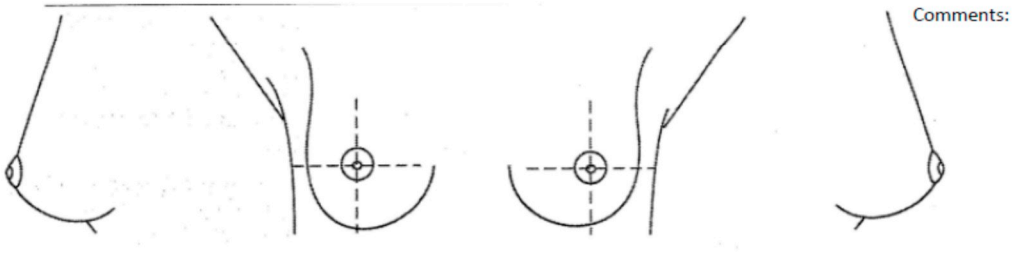
Breast Skin Assessment Form

Affected Breast: Right _____

Left _____

Agent(s) used:

_____



Expanded Radiation Therapy Oncology Group (RTOG) Acute Morbidity Scoring Criteria-Skin

	Upper Medial Quadrant	Upper Lateral Quadrant	Lower Medial Quadrant	Lower Lateral Quadrant	Infra-mammary Fold	Axilla	Subclavicular Area
Skin is normal (No change over baseline)	0	0	0	0	0	0	0
Skin is dry, may be peeling, feel itchy, and have increased pinkness, but not tender (Follicular, faint or dull erythema/ epilation/dry desquamation/ decreased sweating)	1	1	1	1	1	1	1
Skin is pink to rose like a sunburn and tender (Tender or bright erythema, patchy moist desquamation/ moderate edema)	2	2	2	2	2	2	2
Skin is red and may have open areas (Confluent, moist desquamation other than skin folds, pitting edema)	3	3	3	3	3	3	3
Skin is open and may bleed or have black areas (Ulceration, hemorrhage, necrosis)	4	4	4	4	4	4	4

Skin Toxicity Total_____

Fig. 1. Breast Skin Assessment Form (BSAF) was implemented to collect weekly skin toxicity grade in 7 areas in the breast radiation treatment field.

confluent, moist desquamation other than skin folds, pitting edema; and "4" ulceration, hemorrhage, necrosis (RTOG).

2.3.3. Breast Skin Assessment Form (BSAF)

The BSAF is an investigator-developed tool designed to collect the RTOG skin toxicity score for seven areas in the breast radiation treatment field, maximum score, sum of the seven scores, cumulative radiation dose, a line drawing of a breast image, laterality of breast treated, and comment section. The BSAF data collection tool was developed for this study. Using the BSAF, the PI assessed the RTOG score for the upper outer quadrant, upper inner quadrant, lower outer quadrant, lower inner quadrant, and inframammary fold of the breast; axilla, and subclavicular area. These multiple assessments represent the surface area affected by radiodermatitis and allow for examination of skin-related quality of life related to specific anatomical sites in the treatment field. The RTOG score for these seven areas was summed to provide a total score that represents surface area and severity of breast radiodermatitis. These data were collected at baseline, then weekly during radiotherapy. See Fig. 1.

2.3.4. Skin phototype

Skin phototype was determined by the PI during a short interview with the participant. The potential ratings included: type I—always burns, never tans; type II— always burns easily, tans minimally; type III—burns moderately, tans uniformly; type IV—burns minimally, always tans well; type V—rarely burns, tans profusely; and type VI—never burns (Wolff and Johnson, 2009).

2.3.5. Radiation treatment

The radiation treatment plan (i.e., normofractionated, accelerated) was recorded at the start of the study. The cumulative radiation dose, energy, fraction number, and use of a breast immobilizer or bolus pad were recorded weekly. A bolus pad is used to increase the radiation dose to the skin and/or the tissue below the skin (BreastCancer.org, 2014).

2.4. Sample size

Recommended sample size for pilot studies is a contentious topic and suggestions have ranged from 12 subjects per arm to totals of 30 or more subjects (Julious, 2005; Lancaster et al., 2004). We sought sufficient power to accurately detect significant differences in our larger pilot study looking at the impact of radiodermatitis on skin-related quality of life (Beamer and Grant, 2018). A sensitivity analysis using G*Power version 3.1.9.1 (Buchner et al.) was conducted since we did not have an priori estimate of the effect of radiodermatitis on quality of life (Sim and Lewis, 2012). We expected to be able to detect an effect size of 0.18 using a sample size of 40 participants in one group, alpha level of significance = 0.10, power = .80, epsilon = 1.0, correlation = 0.50, and three repeated measurements (Beamer and Grant, 2018). Further, if we were able to follow participants for six repeated measurements, an effect size of 0.15 could be detected. Rubinstein et al. (2005) argued for use of a slightly relaxed level of significance (0.10) to help avoid missing differences that are small but clinically significant in a phase II clinical trial. Similarly, we sought to avoid missing small but

clinically significant differences in this descriptive feasibility and pilot study. All participants gave written informed consent before inclusion in the study and voiced assent during the study.

2.5. Ethical approval

Ethical approval was gained from the University of Utah Institution Review Board (UIRB), Salt Lake City, Utah, USA. A reliance agreement was created between the UIRB and the health care system affiliated with the Centegra Sage Cancer Center. A letter of agreement was signed between the UIRB and the Northern Illinois University IRB, naming UIRB as the IRB of record.

3. Analytic strategy

The IBM Statistical Package for the Social Sciences Statistics for Windows Version 21.0 was used to create a database and analyze the quantitative data collected. Means, standard deviations, and ranges were calculated for continuous data; while frequencies and ranges were determined for categorical data. A one-way within-subjects repeated measures ANOVA was conducted to compare skin toxicity grade of the breast using the RTOG scoring system by each individual area in the radiation treatment field and the total of all scores at baseline and weeks 1, 2, 3, 4, and 5 on external radiotherapy.

Kendall's tau is a nonparametric correlation used instead of a Spearman Rho correlation when the sample size is small and there are tied ranked scores (e.g., RTOG scores by breast site; Field, 2009). Therefore, a Kendall's tau correlation was performed to measure the relationship between factors and the severity of radiodermatitis at five weeks on external radiotherapy of the breast since our sample was small.

4. Results

4.1. Sample

A purposive sample of 41 English-speaking adult women with stage 0-III breast cancer identified as candidates for external beam radiotherapy were accrued to the study from May 2014 through May 2015. One participant withdrew from the study during the first week. The remaining 40 participants were followed from baseline to completion of radiotherapy and completed all study measures. These participants ranged in age from 40 to 82 years. Additional information about the participants is provided in Table 1.

One participant had a history of vitiligo. Her depigmented skin did not develop radiodermatitis. Her normally pigmented skin reacted similarly to other study participants' skin. Another participant had a history of polycystic ovary syndrome. The skin over multiple areas of her body outside of the treatment field was hyperpigmented. This participant also had very large breasts, developed grade 3 skin toxicity in the inframammary fold, and required a 2-day treatment break. A third participant with very large breasts developed grade 3 skin toxicity in the inframammary fold and axilla. She required a 9-day treatment break including 4 weekend days. Her skin was examined at the predetermined weekly study time points and additional times when she came to the cancer center for skin checks. The reported results focus on baseline and five weekly observations since seven participants received accelerated treatments and were unavailable for follow-up observations.

Table 1
Sample characteristics (n = 40).

Age in years		
Mean (Range)	59	(40–82)
SD	11.63	
BMI (kg/m^2)		
Mean (Range)	29	(18.0–52.9)
SD	8.04	
Nipple-to-fold breast length in cm		
Mean (Range)	9.20	(5–19)
SD	2.99	
	Frequency (%)	
Bra cup size		
AA	1	(2.5)
A	2	(5)
B	6	(14)
C	16	(40)
D	7	(17.5)
DD	4	(10)
DDD	1	(2.5)
J	2	(5)
Does not wear a bra	1	(2.5)
Bra band size		
Median	36	(32–44)
Smoking status		
Current smoker	3	(7.5)
Previous smoker	19	(47.5)
Never smoked	18	(45)
Race/Ethnicity		
Non-Hispanic White	39	(97.5)
Asian	1	(2.5)
Skin phototype		
I	8	(20)
II	11	(27.5)
III	11	(27.5)
IV	5	(12.5)
V	5	(12.5)
VI	0	(0)
Stage[a]		
0 (Tis)	7	(17)
I	7	(17)
IIa	15	(36)
IIb	3	(7)
IIIa	4	(10)
IIIb	2	(5)
IIIc	2	(5)
Grade		
1	6	(15)
2	19	(47.5)
3	15	(37.5)
Tumor Histology		
Ductal	28	(70.0)
Lobular	5	(12.5)
DCIS	7	(17.5)
Receptor status		
ER positive	33	(82.5)
PR positive	30	(75)
HER2 positive	9	(22.5)
Surgery		
Lumpectomy	28	(70.0)
Mastectomy with reconstruction	5	(12.5)
Mastectomy without reconstruction	6	(15)
None	1	(2.5)
Systemic therapy (yes)		
Chemotherapy before radiotherapy	22	(55)
Hormone therapy	0	(0)
Trastuzumab	6	(15)

[a] Values are rounded to the nearest whole number.

4.2. Feasibility

Field notes on feasibility and best practices were documented throughout the study. Rates of recruitment, refusal, retention, withdrawal, study measures, and measurements were calculated. The community-based participants were committed to finishing all the measurements if they elected study participation (i.e., 98% retention, 18% refusal rate). Additionally, we had no missing data because the PI returned to the radiation oncology department on subsequent days until all data were collected each week. The results of our assessment of feasibility are presented in Table 2.

Table 2
Assessment of feasibility.

Process	Findings/Recommendations
Recruitment	Recruitment was most successful on the consultation day, moderately successful at the simulation visit, and least successful just prior to treatment on the first day of therapy. It took 13 months to recruit our participants.
What was the refusal rate?	18% (9 of 50 potential participants declined participation). The most frequent reason for refusal was "overwhelmed right now." One woman perceived participation in any study as highly experimental and "beyond imagination."
Can the refusal rate be decreased without coercion?	
What was the retention rate?	98% (Only 1 of 41 participants who consented withdrew).
Can the retention rate be improved?	All participants who remained in the study beyond the baseline time point completed all of the measures.
Eligibility criteria:	
Are there any problems with the eligibility criteria?	Recommend including women with inflammatory breast cancer who are post-mastectomy, males, and transgender females with breast cancer. Recommend including individuals with certain conditions affecting skin pigmentation such vitiligo and polycystic ovary syndrome.
Measures	The income range on the demographics form should extend higher than $75,000 USD per year.
Are there any problems with the instruments?	Create a breast skin assessment form with a mastectomy image. Consider adding an image of a back on the breast skin assessment form. RTOG Acute Radiation Morbidity Scoring Criteria does not clearly delineate between erythema and patchy moist desquamation.
Resources	**Findings/Recommendations**
Determine capacity and identify best practices	Assessing for skin toxicity in the treatment vault during set-up for treatment prevented the need to use an exam room and saved the participant from needing to undress for the study. Investigator had a pre-existing working relationship with the radiation oncology team. That enhanced trust and cooperation. Conducting study assessments every Monday worked well in a department operating Monday-Friday. This allowed 4 days in a row (i.e., Tuesday through Friday) to capture any missed assessments. On rare occasions, patients would request a one-time change in appointment time. The PI was not informed of these changes since she was not employed at the cancer center and this led to missed assessments on Mondays requiring extra trips to the cancer center.
Does the center adhere to promises?	No problems identified
Management	Findings/Recommendations
What qualifications are needed by the PI?	Researcher or research assistant/associate needs to be familiar with and work in the radiation oncology department, and have dedicated time for the study (e.g., all study measures, data management).
Are there improvements needed to enhance management of the study?	Scannable data forms would likely enhance data accuracy and save time.
Scientific	Findings/Recommendations
Can effect sizes be calculated and to which populations do they apply?	Calculating effect sizes (ES) to inform future power analyses is helpful. Care must be taken to avoid over- relying on the ES from a study that is not identical to your own.

4.3. Piloted measures & outcomes

We piloted two measures that might improve ability to predict or measure skin toxicity (i.e., clinician-measured breast length, 7 measurements of skin toxicity in the radiotherapy treatment field). Accurately identifying risk factors for breast radiodermatitis is important for studies of measures that may prevent or manage that toxicity.

4.3.1. Clinician-measured breast length

A comparison of participant-reported bra cup size and clinician-measured breast length is presented in Table 3. The current standard measure participant-reported bra cup size was compared to measured breast length, a new measure. Bra cup sizes and measured breast lengths were discordant in this study. For example, a woman with a breast length of 5 cm reported wearing a C cup, while another woman with a 6.5 cm breast length wore an AA-sized bra cup. Women with 10.5 cm breast lengths reported wearing a D, DD, or DDD-sized bra cup.

Table 3
Comparison of participant-reported bra cup size and clinician-measured breast length.

Bra Cup Size	n	Breast Length in cm (range)
AA	1	6.5
A	2	5.0–7.0
B	6	6.0–8.0
C	16	5.0–12.5
D	7	7.5–10.5
DD	4	10.5–19
DDD	1	10.5
J	2	14.0–15.0
Does not wear a bra	1	10.5

4.3.2. Maximum skin toxicity

The mean and standard deviation of skin toxicity scores was calculated at baseline, then during week 1 through 5 on radiotherapy. These results are presented in Table 4.

Table 4
Descriptive statistics for radiation-induced skin maximum toxicity of the breast at baseline and weeks 1–5 on radiotherapy[a].

Time Period	n	*M*	(SD)
Baseline (before RT)	40	.00	(.00)
Week 1 on RT	40	.10	(.30)
Week 2 on RT	40	.60	(.67)
Week 3 on RT	40	1.08	(.69)
Week 4 on RT	40	1.45	(.55)
Week 5 on RT	40	1.85	(.48)

Abbreviations: RT = Radiotherapy, *n* = number of participants assessed, *M* = mean, SD = standard deviation.

[a] The RTOG Acute Radiation Morbidity Scoring Criteria-Skin was used to measure maximum skin toxicity. The ratings range from "0" no change over baseline; "2" tender or bright erythema, patchy moist desquamation/moderate edema; "3" confluent, moist desquamation other than skin folds, pitting edema; and "4" ulceration, hemorrhage, necrosis.

Table 5
Summary table for within-subjects repeated measures analysis of variance of radiodermatitis of the breast by site in the treatment field.

Time	*M*	SD	Wilkes λ	F	DF*	*p*	η^2
Upper Medial Quadrant			.23	23.90	(5,35)	< .001	.77
Baseline	.00	.00					
Week 1	.03	.16					
Week 2	.13	.40					
Week 3	.50	.68					
Week 4	.68	.73					
Week 5	1.18	.68					
Upper Lateral Quadrant			.16	35.72	(5,35)	< .001	.84
Baseline	.00	.00					
Week 1	.05	.22					
Week 2	.25	.54					
Week 3	.65	.70					
Week 4	.70	.69					
Week 5	1.23	.62					
Lower Medial Quadrant			.18	32.87	(5,35)	< .001	.82
Baseline	.00	.00					
Week 1	.03	.16					
Week 2	.23	.48					
Week 3	.63	.67					
Week 4	.80	.79					
Week 5	1.13	.61					
Lower Lateral Quadrant			.16	37.07	(5,35)	< .001	.84
Baseline	.00	.00					
Week 1	.08	.27					
Week 2	.15	.36					
Week 3	.73	.68					
Week 4	.95	.78					
Week 5	1.20	.61					
Inframammary Fold			.12	66.97	(5,35)	< .001	.88
Baseline	.00	.00					
Week 1	.00	.00					
Week 2	.23	.48					
Week 3	.78	.66					
Week 4	1.25	.67					
Week 5	1.58	.64					
Axilla			.11	56.97	(5,35)	< .001	.89
Baseline	.00	.00					
Week 1	.03	.16					
Week 2	.15	.36					
Week 3	.43	.71					
Week 4	.93	.69					
Week 5	1.60	.59					
Subclavicular Area			.40	10.60	(5,35)	< .001	.60
Baseline	.00	.00					
Week 1	.03	.16					
Week 2	.28	.55					
Week 3	.48	.75					
Week 4	.65	.74					
Week 5	1.00	.85					
Total for all Sites			.10	65.22	(5,35)	< .001	.90
Baseline	.00	.00					
Week 1	.23	.86					
Week 2	1.40	2.04					
Week 3	4.08	3.34					
Week 4	5.95	3.65					
Week 5	8.85	3.08					

Abbreviations: M = mean, SD = standard deviation, DF = degrees of freedom (hypotheses, error), n^2 = eta squared.

4.3.3. Multiple measurements of skin toxicity

A one-way within-subjects repeated measures ANOVA was conducted to compare skin toxicity grade of the breast using the RTOG scoring system for each individual area in the radiation treatment field and the total of all scores at baseline and weeks 1, 2, 3, 4, and 5 on external radiotherapy. The results are presented in Table 5. The maximum skin toxicity score significantly increased with time on radiation treatment, Wilk's Lambda = 0.05 F (5, 35) = 132.07, p < .00001, multivariate partial eta squared = 0.95. There was a significant effect size (η2) for time in each area in the treatment field, ranging from η2 0.60 to 0.89 with the smallest effect in the subclavicular area and the largest effect in the axilla. The effect of time on the total toxicity score for all areas was η2 = 0.90, p < .001. Overall, 20% of the participants experienced grade 1, 75% had grade 2, and 5% suffered grade 3 skin toxicity at five weeks on treatment.

4.4. Risk factors for radiodermatitis

The relationship between potential risk factors and the severity of radiodermatitis at five weeks on external radiotherapy of the breast was measured using Kendall's tau correlation. The results are presented in Table 6. As expected, there were a number of significant correlations between severe radiodermatitis in one area and another area of the breast. For example, if radiodermatitis increased in one breast quadrant, it significantly increased in all other quadrants, supporting the need for multiple measurements of skin toxicity. Radiodermatitis severity in the inframammary fold was significantly associated with increased severity in the lower, but not upper breast quadrants.

4.4.1. Biometrics

As body mass index increased, skin toxicity significantly increased in the inframammary fold (r = 0.32, p = .01) and axilla (r = 0.26, p = .05). An increase in bra cup size correlated with an increase in maximum RTOG score at five weeks on radiotherapy (r = .29, p = .04), upper medial breast quadrant (r = 0.29, p = .04), lower lateral quadrant (r = 0.30, p = .02), inframammary fold (r = 0.41, p = .004), and BMI (r = 0.42, p = .005). Breast length was associated with an increase in RTOG score (r = 0.28, p = .04), upper medial breast quadrant (r = 0.28, p = .04), upper lateral quadrant (r = 0.30, p = .02), lower lateral quadrant (r = 0.30, p = .02); and a highly significant association with inframammary fold (r = 0.45, p = .001), increasing BMI (r = 0.41, p = .002), and bra cup size (r = 0.57, p = .0003). Overall, breast length had a greater number of highly significant correlations. This suggests that breast length may have an equivalent or stronger relationship with radiodermatitis severity as compared to bra cup size.

4.4.2. Skin phototype

Race and ethnicity did not have any significant correlations in our nearly all White study population. However, as skin phototype (i.e., sunburn resistance) increased, radiodermatitis in the inframammary fold also significantly increased (r = .34, p = .02). This suggests that skin phototype might be able to discriminate between skin types among individuals of the same race.

5. Discussion

5.1. Clinician-measured breast length

We proposed the concept of clinician-measured breast length for this feasibility study because studies have shown that bra cup size is not a reliable proxy for actual breast size. As illustrated in Table 3, participant-reported bra cup size was discordant with clinician-measured breast length, which is a more scientific alternative to participant-reported bra cup size. Breast length was significantly positively correlated with radiodermatitis in the inframammary fold and upper medial, upper lateral, and lower lateral breast quadrants in this study. Similarly, Porock et al. (1998) found bra cup size greater than size C predicted an RTOG skin toxicity score of 2 or higher in the inframammary fold, upper outer quadrant, upper inner quadrant, lower outer quadrant, and lower inner quadrant of the breast radiotherapy treatment field. Pires et al. (2008) measured breast height (i.e., distance from the chest wall to nipple measured on a contour plan) and found that each centimeter of increased height increased the chance of developing grade 3 skin toxicity by 2.61-fold. Overall, these findings support the importance of breast size as a risk factor for radiodermatitis.

Measuring the breast length takes only a few seconds and is not costly since disposable measuring tapes are inexpensive (e.g., 15 cents

Table 6
Variables related to the severity of radiation dermatitis at week 5 among women receiving breast radiotherapy.

	Measure	1	2	3	4	5	6	7	8	9	10	11	12
1	RTOG Score	__											
2	Upper Medial	.45[b]	__										
3	Upper Lateral	.37[a]	.38[b]	__									
4	Lower Medial	.39[b]	.66[b]	.55[b]	__								
5	Lower Lateral	.43[b]	.53[b]	.57[b]	.43[b]	__							
6	Inframam Fold	.65[b]	.21	.22	.53[b]	.48[b]	__						
7	Axilla	.61[b]	.49[b]	.26	.57[b]	.44[b]	.53[b]	__					
8	Subclavicular	.18	.08	.05	.77[b]	.13	.12	.26	__				
9	Skin Type	.18	.18	.18	.19	.09	.34[a]	.21	-.02	__			
10	BMI	.15	.15	.13	.13	.22	.32[a]	.26[a]	-.05	-.06	__		
11	Bra Cup Size	.29[a]	.29[a]	.19	.19	.31[a]	.41[b]	.22	-.16	.07	.42[b]	__	
12	Breast Length	.28[a]	.28[a]	.30[a]	.23	.30[a]	.45[b]	.16	-.01	.18	.41[b]	.57[b]	__

Abbreviations: Inframam Fold = inframammary fold, BMI = body mass index.
[a] Correlation is significant at the 0.05 level (2-tailed).
[b] Correlation is significant at the 0.01 level (2-tailed).

US) and the measurement can be completed by a registered nurse or trained research associate. Conversely, breast volume calculation by a radiation oncologist or medical physicist on a contour plan is a more expensive alternative to clinician-measured breast length. To provide a context, Caruso et al. (2006) compared the cost of using a manual measurement of breast volume (i.e, Grossman Roudner breast-measuring device, breast casting) against medical resonance imaging (MRI) to objectively estimate increase in breast size after application of topical compounds as an alternative to breast augmentation surgery. Use of MRI was 373 to 33,500 times more expensive than the manual method of measuring breast volume (Caruso et al., 2006).

Clinician-measured breast length may prove an effective predictor of radiodermatitis instead of, or in addition to, participant-reported bra cup size. However, evidence regarding the comparative effectiveness of clinician-measured breast length, a new measure, versus participant- or client-reported bra cup size, the current standard, is still needed.

5.2. Maximum skin toxicity

Several significant findings were identified. As expected, the maximum skin toxicity (i.e., RTOG) score significantly increased with time on radiotherapy and the mean score at five weeks on radiotherapy was 1.85. Moreover, skin toxicity significantly increased with time on radiotherapy in every site in the radiation treatment field. More importantly, by implementing multiple assessments of skin toxicity, our results showed a mean RTOG score of more than 1.0 in all areas of the treatment field, including 1.58 in the inframammary fold, and 1.60 in the axilla at five weeks on radiotherapy. A grade 1 acute skin toxicity may include dry desquamation, while grade 2 may include patchy moist desquamation and is considered a moderate to severe toxicity (Sharp et al., 2011).

5.3. Multiple measurements of skin toxicity

We measured the maximum grade of skin toxicity in 7 areas of the breast treatment field weekly during radiotherapy and summed these scores each week. The mean of the summed RTOG scores for all seven sites in the treatment field was 8.85, much higher than a single measurement of the maximum skin toxicity. The clinical significance of these summed scores remains to be determined. However, the individual toxicity score for site in the treatment field combined with skin-related QOL might be useful for testing the efficacy of a radiodermatitis prevention or management intervention for that specific treatment site. For example, an agent may work well on the surface of a breast quadrant but not in the inframammary fold or vice versa. Finally, assessing dermatitis in multiple areas within the radiation treatment field can be performed quickly when the data is entered on a standardized form such as the BSAF.

5.3.1. Strengths and limitations

This study has several strengths. For example, accrual goals were met. There was only one rater of skin toxicity, eliminating the issue of interrater reliability. However, threats to intrarater reliability include fatigue, time of day, attention (Laerd Dissertation). Each woman served as her own control eliminating between-subjects variance. We tested and reported the feasibility of our measures planned for use in future studies. Study limitations include a small sample size with limited diversity. The sample was limited to English-speaking women since the researcher speaks only English.

6. Conclusions

This pilot and feasibility project enabled us to identify several recommendations that will be important in similar future research studies. For example, performing assessments on Mondays allowed for follow-up on Tuesday through Friday to collect missing information for a given week in a radiation oncology department operating Monday through Friday. Ideally, future investigators or research staff should be onsite daily to facilitate recruitment and collection of time-sensitive data. Our BSAF data collection form for seven areas in the breast radiation treatment field worked well but might be improved by adding an image of the posterior surface of the chest. Creating a form with an image of mastectomy without reconstruction (i.e., chest wall) would also aid in mapping radiodermatitis. Additional studies are needed to determine the clinical significance of the total RTOG score for all areas in the radiation treatment field.

We wondered whether community-dwelling women with breast cancer would allow measurement of their breast length. No participant refused this one-time measurement. Moreover, the cost was negligible. The utility of clinician-measured breast length and multiple measurements of skin toxicity in the treatment field must be tested in larger studies and more diverse populations. However, it was feasible to complete these study measurements in a community cancer program setting.

The results of studies examining methods to prevent or manage radiodermatitis are inconsistent. Standardizing measures and measurements in clinical trials would improve comparability between studies. Clinician-measured breast length in place of or in addition to participant-reported bra cup size may provide greater precision in predicting risk of developing breast radiodermatitis. Mapping skin toxicity in the breast radiation field may allow mapping of response to interventions designed to prevent or manage radiodermatitis. A data collection form such as the BSAF would enhance this mapping. Preventing and managing radiodermatitis is crucial to maintaining

quality of life, avoiding treatment breaks, and enhancing survival.

Conflicts of interest

The author declares she has no conflicts of interests.

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