

Response Form for the Final Performance Review Report*

1. Name of Grantee: American College of Radiology
2. Year of Grant: 2008 Formula Grant

A. For the overall grant, briefly describe your grant oversight process. How will you ensure that future health research grants and projects are completed and required reports (Annual Reports, Final Progress Reports, Audit Reports, etc.) are submitted to the Department in accordance with Grant Agreements? If any of the research projects contained in the grant received an “unfavorable” rating, please describe how you will ensure the Principal Investigator is more closely monitored (or not funded) when conducting future formula funded health research.

1. The American College of Radiology has a Management & Scientific Oversight (MSO) Board that meets quarterly to review the progress of all ACR CURE projects and, in conjunction with senior scientific leadership of the research groups, review all formula grant proposals.
Their responsibilities include:
 - a. Review proposals/reports prior to submission.
 - b. Work with the national leadership of the research groups (ACRIN and RTOG) to provide high-level scientific review of project proposals and ongoing progress.
 - c. Convene quarterly meetings to review project progress; if insufficient progress is noted, an action plan will be required.
 - d. Evaluate if closure or project reassignment is warranted for projects where there has been insufficient progress. Make appropriate recommendations to the responsible group PI.
 - e. Document minutes and action items of each meeting.
2. The American College of Radiology has a dedicated program manager; the manager is responsible for ensuring that ACR’s CURE projects are completed and the required reports are submitted in accordance with the requirements of the CURE program.
Responsibilities of the program manager:
 - a. Responsible for submission of all CURE applications, annual and final reports
 - b. Facilitate quarterly CURE MSO Board meetings and work with the finance department and project PIs to provide the reporting tools needed to monitor and track each project’s progress.
 - c. Serve as liaison to the Pennsylvania Department of Health CURE program staff.
 - d. In conjunction with the ACR finance department, monitor expenditures to insure that they are appropriate for each project’s progress and that the budget continues to reflect project aims.

* Please note that for grants ending on or after July 1, 2007, grantees’ Final Performance Review Reports, Response Forms, and Final Progress Reports ***will be made publicly available on the CURE Program’s Web site.***

3. Additional oversight:
 - a. Applications and Final Reports are peer reviewed by individuals with the appropriate background as related to a project.
 - b. Clinical trials are overseen by the Data Safety Monitoring Boards of each group, with meetings at least semiannually
 - c. Minimal start-up funds are made available to an investigator for legitimate expenses projected prior to the project's first progress report. For the remainder of the project, reimbursement is made for documented work completed and/or milestones met, and upon submission of the required CURE annual progress report.

Project Number: **0862401**

Project Title: Methods and Strategies to Incorporate Radiotherapy Delivery Uncertainties in Clinical Trials Outcome Analysis

Investigator: Xiao, Ying

B. To ensure that feedback provided in the Final Performance Summary Report is utilized to improve ongoing and future research efforts, briefly describe your plans to address each specific weakness and recommendation as noted in Section B of the Final Performance Summary Report and listed below. If no weaknesses are listed below, no response is required.

(As you prepare your response please be aware that the Final Performance Summary Report, this Response Form, and the Final Progress Report will be made publicly available on the CURE Program's Web site.)

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

The results are compelling and the methodology and new insights could be useful in NCTN trials (a grant application has been submitted for funding the Imaging Core), but it is not entirely clear from the application how this will be done.

Response: We thank the reviewer for a positive review of the study conduct. The methodology developed from this study has been adopted for quality assurance of NCTN trials as included in the grant submission of Imaging and Radiation Oncology Core (IROC) of NCTN. Funding for the IROC grant began March 1, 2014.

Reviewer 2:

None.

Reviewer 3:

1. One weakness of this project was that the original objectives were somewhere between difficult and impossible to achieve, at least within the budget and the time period. The main accomplishments were not in clinical trials outcome assessment, but in quantification and investigation of uncertainties in radiotherapy. This is in itself valuable, and perhaps the proposal would have appeared more realistic if it focused on that area.

Response: The original objectives were indeed too broad and ambitious. We tailored what was realistically achievable and performed the study to the best of the resource allowed.

2. If one did want to model the impact of dose uncertainty in clinical trials, then much better data need to be utilized. We would need the planned dose, the actual dose (estimated) both to the tumor and to sensitive surrounding tissues (lung, heart, gut, bladder, etc., depending on the tumor), and then outcome data, both in tumor response and in adverse events. This is feasible with substantial advance planning and the cooperation of the trial organizers. This could be of great value.

Response: We agree. Future projects will be more sophisticated, e.g. as described in the comment.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response: N/A

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response:

Project Number: **0862402**

Project Title: Development and Analysis of an Infrastructure for
Review of Modern Clinical Trials that Include Radiotherapy

Investigator: O'Meara, Elizabeth

B. To ensure that feedback provided in the Final Performance Summary Report is utilized to improve ongoing and future research efforts, briefly describe your plans to address each specific weakness and recommendation as noted in Section B of the Final Performance Summary Report and listed below. If no weaknesses are listed below, no response is required.

(As you prepare your response please be aware that the Final Performance Summary Report, this Response Form, and the Final Progress Report will be made publicly available on the CURE Program's Web site.)

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

None.

Reviewer 2:

1. The project has so far not published or disseminated its findings appropriately. This is a significant weakness given that the point of developing case review tools for radiotherapy trials is so that the community can benefit from them. The project needs to publish the variety of comparative case review studies it has performed so far.

Response: The objective of the project was to build infrastructure for case review with advanced technology, which we successfully accomplished.

2. The project's strategic plan described the generation of training modules for study PIs to prepare them for the case review process. These do not appear to have been created, and should be and should be disseminated as should the recommendations for case review procedures.

Response: We have been using benchmark cases for trials to train and credential PIs.

We have detailed instructions that we disseminate to PIs on a wide array of subjects ranging from how to obtain remote review user accounts to how to use the applications for conducting the review. We usually offer one on one training sessions for those PIs who are not already familiar with the system.

Reviewer 3:

While the investigators stated up front that the goal of the research which was to examine time and efficiency of submitted clinical trial cases, it would have certainly been of interest to document their efficiency rather than stating it was just obvious. Certainly, they could have compared process and software to assess this along with other parameters such as the time

involved for the submitting physician to achieve a suitable plan and submit it. Efficiency should be extended to the design of the clinical trial radiation parameters to make trials easier to plan and submit. Some trials have radiation parameters that are very difficult to achieve at the time of planning and research such as this could help make accruals easier.

Response: Efficiency is definitely a continuous goal of the conduct of quality assurance of clinical trials. We have implemented the centralized remote review capability.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response: N/A

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response:

Project Number: 0862403

Project Title: Screening For Depression and Referral for Treatment of Cancer Patients

Investigator: Watkins-Bruner, Deborah

B. To ensure that feedback provided in the Final Performance Summary Report is utilized to improve ongoing and future research efforts, briefly describe your plans to address each specific weakness and recommendation as noted in Section B of the Final Performance Summary Report and listed below. If no weaknesses are listed below, no response is required.

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SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

1. Utilized cut-off scores should be reported for each screening instrument with evidence-based rationale. Which score was used for referral to diagnostic interview?

Response: The following cut-off scores were used to determine depression:

PQ-9 > 9,
PQ-2 > 2, and
HSCL-25 > 43.

2. The number of baseline clinical interviews (SCIDs) attempted and completed should also be reported with calculations for sensitivity, specificity, positive predictive values, and negative predictive values per the primary screening instrument. The prevalence of each depressive disorder should be reported. The additional screening instruments should also be examined in association to diagnoses, given they are most commonly used instruments (PHQ9, PHQ2, distress thermometer). How much incremental validity is estimated by longer instruments? How does incremental validity compare to resource utilization per instrument? How many patients were already receiving treatment?

Response: The following table provides information on the SCIDs:

Number of Stage II SCID Interviews Required – All patients*	(n=150)
Interview completed	79 (52.4%)
Not evaluated, patient contacted, declined interview	10 (6.7%)
Not evaluated, temporary IRB hold on contact attempts	18 (12.1%)
Not evaluated, patient unable to be contacted	38 (25.5%)
Unknown†	5 (3.3%)

†According to patient tracking, these patients should have received interviews but the interviewers did not track status of interview

The table below details how patients were screened by tool. Please note that NCCN-DT was collected but not used to determine depression for referral to a diagnostic interview.

Baseline Screenings
(n=455)

PHQ-9	
Negative	414 (91.0%)
Positive	41 (9.0%)
PHQ-2	
Negative	419 (92.1%)
Positive	36 (7.9%)
NCCN-DT	
Negative	305 (69.5%)
Positive	134 (30.5%)
HSCL-25	
Negative	386 (84.8%)
Positive	69 (15.2%)

The table below contains information on depressive/mood disorders. This data by screening instrument was not examined in this analysis.

Depressive Disorders
(n=79)

Depressed/Mood Disorder	
No	64 (81.0%)
Yes	15 (19.0%)
Hypomania	
No	79 (100.0%)
Mania	
No	79 (100.0%)
Dysthymic	
No	77 (97.5%)
Yes	2 (2.5%)
Adjustment	

**Depressive Disorders
(n=79)**

No	73 (92.4%)
Yes	6 (7.6%)
Major Depression	
No	70 (88.6%)
Yes	9 (11.4%)
GMC/Substance Causing Symptoms	
No	79 (100.0%)

The sensitivity, specificity, false negative rate, and false positive rate are given in the table below:

Evaluation of Screening Questionnaires

	n	False Negative Rate [1-Sensitivity]	False Positive Rate [1-Specificity]	True Positive Rate [Sensitivity]	True Negative Rate [Specificity]
Patient Health Questionnaire, 9-item [PHQ-9]	79	0.33	0.22	0.67	0.78
Hopkins Symptom Checklist, 25-item [HSCL-25]	79	0.13	0.42	0.87	0.58
Patient Health Questionnaire, 2-item [PHQ-2]	79	0.33	0.14	0.67	0.86
PHQ-9 or HSCL-25	79	0.07	0.44	0.93	0.56
National Comprehensive Cancer Network Distress Thermometer [NCCN-DT]	77	0.20	0.48	0.80	0.52

A question was raised: How does incremental validity compare to resource utilization per instrument?

Response: This was not an aim of this research and beyond the scope of the award.

- The number of follow-up interviews attempted and completed should be reported at proposed 3-month time point. The percentages of patients that experienced increased, decreased and stable depressive symptoms should be reported along with specific evidence-based criteria (e.g., change score, number of points) that signifies clinically significant change.

Response: Due to an IRB hold, 3 of 15 3-month follow-up interviews were not able to be collected. Therefore, no analysis was done using this data.

4. An opportunity exists with this study to describe the investigator team's handling of IRB concerns leading to development of a protocol to protect suicidal patients. What protocol was accepted by all IRBs? How many patients endorsed suicidal ideation? Number of actual suicides and lost to follow-up?

Response: There were 2 types of risk reports: emergent and non-emergent. Non-emergent risk reports were required to be filed if a patient scored ≥ 65 on the HSCL-25 or 20-27 on the PQ-9 with no suicidal ideation. Emergent risk reports were filed if a score of 3-4 on item 23 of the HSCL-25, "Thoughts of ending your life" or a score of 1-3 on item 9 of the PQ-9, "Thoughts that you would be better off dead, or of hurting yourself in some way" were reported, regardless of total score. Emergent risk reports were filed for 13 patients with 4 (30.8%) patients having suicidal ideation.

There was no follow-up data collection by the institution with respect to number of suicides or patients lost to follow-up.

The IRB approved protocol was already submitted in past progress reports but below is the specific section on safety that was approved. The performance reviewers' recommendations and our responses to the recommendations resume on page 18.

APPENDIX V (12/7/09) (5/27/10)

SAFETY PLAN

1. Assessment of Risk of Self-Harm (Suicide)

2. Emergent Risk and Non-Emergent Risk Incident Reports

SAFETY PLAN: Assessment of Risk of Self-Harm (Suicide)

Questionnaires and telephone interviews administered per this protocol contain questions that assess suicidal ideation. Study participants may self-report suicidal ideation at the time of Stage I Screening, during Stage II Telephone Interviews or at Stage III Follow-up Telephone Assessment. When suicidal ideation is reported, the risk of self-harm must be assessed. This Safety Plan provides detailed instructions on identifying reported suicidal ideation and subsequent steps to assess and manage risk of self-harm. This Safety Plan also provides instructions on how to respond to participants that report elevated levels of distress in the absence of suicidal ideation.

Stage I Screening: HSCL-25 and PHQ-9/PHQ-2

Participants complete the HSCL-25 and the PHQ-9/PHQ-2 at Stage I Screening. Both questionnaires contain items that assess thoughts about suicide. Staff at RTOG member institutions will be required to review completed questionnaires and respond in accordance with

this Safety Plan in the event that suicidal ideation and/or elevated distress is reported through responses to specific questionnaire items.

1. HSCL-25:

Item 23 Suicidal thoughts:

A score of 3 or 4 on item 23 (Thoughts of ending your life) will trigger the Emergent Risk Policy (see below).

Elevated distress:

A total score of 65 or greater in the absence of suicidal ideation (a score of 1 on item 23) will trigger the Non-emergent Risk Policy (see below).

2. PHQ-9:

Item 9 Suicidal thoughts:

A score of 1, 2, or 3 on item 9 will trigger the Emergent Risk Policy (see below).

Elevated distress:

A total score of 20 or greater in the absence of suicidal ideation (score of 0 on item 9) will trigger the Non-emergent Risk Policy (see below).

Stage I Screening Emergent Risk Policy

Participants who report suicidal thoughts on the HSCL-25 or PHQ-9 are required to undergo evaluation by a clinician in the patient's cancer care setting to assess degree of risk. If a participant meets criteria for this, notify clinical staff immediately that the patient requires a risk assessment prior to leaving the clinic.

The Informed Consent gives us permission to share information so reporting suicidality is not a breach of confidence. Once clinical staff have been notified, your responsibility has been discharged.

As soon as the site CRA completes the study assessment he or she must complete an Emergent Risk Incident Report and submit it to RTOG.

SAFETY PLAN: Assessment of Risk of Self-Harm (Suicide)

Stage I Screening Non-Emergent Risk Policy

Staff at RTOG member institutions will be required to review completed questionnaires and respond in accordance with this Safety Plan in the event that elevated distress is reported on the HSCL-25 and/or the PHQ-9.

If the HSCL-25 ≥ 65 and/or PHQ-9 ≥ 20 :

This policy requires you to offer referral information to the participant, offering assistance to the patient in obtaining further evaluation and treatment and completion of a Non-Emergent Risk Incident Report.

1. Complete the interview with the participant.
2. Notify the participant that you can provide them with information about where they can receive support. Use the following script:

"On your questionnaire you reported that you were feeling distressed. I wanted you to know that there are individuals at the cancer center where you are being treated or in your community who are trained to help patients with these issues. It's entirely up to you whether you contact these folks or not, but I wanted you to know that support is available if you'd like it. Would you like to speak with someone? I can either ask a member of your oncology health care team to speak with you or I can give you a list of phone numbers for people who have expertise in dealing with people who have distress."

3. If the participant indicates they would like this information and they agree to speak with someone from their oncology health care team, inform the appropriate clinical staff. If the participant indicates that they would like a referral for service in their community, provide the participant with the Psychosocial Care Referral List completed for your institution (available through the RTOG SFTP site). Participants should be offered resources at the site where they are receiving cancer care (if available) as well as community resources.

As soon as the site CRA completes the study assessment he or she must complete the Non-Emergent Risk Incident Report and submit it to RTOG.

Stage II Evaluation and Stage III 3-Month Follow-up Telephone Assessment: SCID, HSCL-25, and PHQ-9/PHQ-2

Participants complete the SCID at Stage II Evaluation and they complete the SCID, the HSCL-25, and the PHQ-9/PHQ-2 at 3-Month Follow-up Assessment. The structured interview and both questionnaires contain items that assess thoughts about suicide. Telephone interviewers will be required to respond in accordance with this Safety Plan in the event that suicidal ideation and/or elevated distress is reported through responses to specific interview and questionnaire items.

1. HSCL-25:

Item 23 Suicidal thoughts:

A score of 3 or 4 on item 23 (Thoughts of ending your life) will trigger the Emergent Risk Policy (see below).

Elevated distress:

A total score of 65 or greater in the absence of suicidal ideation (a score of 1 on item 23)

will trigger the Non-emergent Risk Policy (see below).

2. PHQ-9:

Item 9 Suicidal thoughts:

A score of 1, 2, or 3 on item 9 will trigger the Emergent Risk Policy (see below).

Elevated distress:

A total score of 20 or greater in the absence of suicidal ideation (score of 0 on item 9) will trigger the Non-emergent Risk Policy (see below).

3. SCID:

Module A Mood Episodes criteria 9 asks: “were things so bad that you were thinking a lot about death or that you would be better off dead? What about thinking of hurting yourself?”

A score of 3 with suicidal ideation, specific plan, or suicide attempt qualifiers will trigger the Emergent Risk Policy (see below).

A score of 3 with thoughts of own death outcome and in the absence of suicidality qualifiers will trigger the Non-emergent Risk Policy (see below).

Stage II Evaluation and Stage III 3-Month Follow-Up Emergent Risk Policy

Participants who report suicidal thoughts on the SCID, HSCL-25, or PHQ-9 are required to undergo further evaluation by the telephone interviewer. The telephone interviewer will be required to assess the extent and risk and whether the participant is at risk for self-harm. If a participant reports suicidal ideation, plan and intent:

Inform the participant that you are required by law, as a psychologist, to request further assessment based on some of their responses to the questionnaires. Use the following script as a guide:

"During the interview you reported some thoughts about death or harming yourself that concern me. By law, I'm required to contact 911 to request an urgent assessment by a health care provider unless you agree to contact the emergency room or go to your nearest emergency room."

1. If the participant agrees to contact or go to their nearest emergency room, ask the participant for the name of the hospital. Ask the participant to confirm that they agree to contact or go to an emergency room for further assessment.
2. If the participant refuses, inform the participant that you are required to notify 911 and that you will provide 911 with the participant's contact information, including their home address. Ask the participant to decide whether they wish to initiate contact with 911 or the emergency room or if the interviewer should notify 911. If

the participant continues to refuse to initiate contact, call 911 and provide the participant's name, contact information, and address which is available through the RTOG SFTP site.

The Informed Consent gives us permission to share information so reporting suicidality is not a breach of confidence. Once clinical staff has been notified, your responsibility has been discharged.

As soon as the SCID interview is completed, the interviewer must complete an Emergent Risk Incident Report and submit it to RTOG.

Stage II Evaluation and Stage III 3-Month Follow-Up Non-Emergent Risk Policy

Telephone interviewers will be required to respond in accordance with this Safety Plan in the event that elevated distress is reported on the SCID, the HSCL-25, and/or the PHQ-9.

If participants report elevated distress on the SCID and/or if the HSCL-25 \geq 65 and/or PHQ-9 \geq 20:

This policy requires you to offer referral information to the participant, offering assistance to the patient in obtaining further evaluation and treatment and completion of a Non-Emergent Risk Incident Report.

1. Complete the interview with the participant.
2. Notify the participant that you can provide them with information about where they can receive support. Use the following script:

"During your interview you reported that you were feeling distressed. I wanted you to know that there are individuals at the cancer center where you are being treated or in your community who are trained to help patients with these issues. It's entirely up to you whether you contact these folks or not, but I wanted you to know that support is available if you'd like it. Would you like to speak with someone? I can either ask a member of your oncology health care team to speak with you or I can give you a list of phone numbers for people who have expertise in dealing with people who have distress."

3. If the participant indicates they would like this information and they agree to speak with someone from their oncology health care team, provide the participant with the Psychosocial Care Referral List completed for the institution at which they are receiving care (available through the RTOG SFTP site). Participants should be offered resources at the site where they are receiving cancer care (if available) as well as community resources.

As soon as the SCID interview is completed, the interviewer must complete the Non-Emergent Risk Incident Report and submit it to RTOG.

Emergent Risk Incident Report

Note: This form must be submitted within 1 business day after completion of the questionnaire and/or interview.

Case Number: _____

Date: _____

What triggers Emergent Risk?

-Score on HSCL Item 23 (Thoughts that you would be better off dead, or thoughts of ending your life): A score of 3 or 4 (circle one) requires completion of the Emergent Risk Incident Report and following Section 11.2.2 in the protocol.

-Score on PHQ-9 (Thoughts that you would be better off dead, or thoughts of hurting yourself in some way): A score of 1, 2, or 3 (circle one) requires completion of the Emergent Risk Incident Report and following Section 11.2.2 in the protocol.

Did participant agree to contact with clinical staff for further assessment? Yes
 No

On-Site Clinical Personnel Contacted:

Name of On-Site Clinical Staff: _____

- Yes – Time of contact _____
- No

Emergency 911 contact required?

- Yes – Time of contact _____
- No

Participant Expressed (details):

- Thoughts of own death: _____
- Desire for death/Life not worth living: _____
- Suicidal ideation: _____
- Plan for suicide: _____

Did participant desire contact information for counseling or other mental health treatment? Yes

No

Was information provided?

Yes

No

Signature of Interviewer: _____ **Date:** _____

Check one:

_____ **Stage I Screening**

_____ **Stage II Telephone Interview**

_____ **Stage III 3-Month Follow-Up Interview**

Fax completed form to RTOG Headquarters (215-940-8830).

Non-Emergent Risk Incident Report

Note: This form must be submitted within 2 business days after completion of the questionnaire and/or interview.

Case Number: _____

Date: _____

Participant Expressed (details):

- HSCL \geq 65**
- PHQ \geq 20**
- SCID: Elevated distress reported**

Score on HSCL Item 23 (Thoughts of ending your life) - If the score is 3 or 4, then fill out the Emergent Risk Incident Report and follow Section 11.2.2 in the protocol: _____

Score on PHQ-9 (Thoughts of hurting yourself in some way) - If the score is 1, 2, or 3, then fill out the Emergent Risk Incident Report and follow Section 11.2.2 in the protocol: _____

On-Site Clinical Personnel Contacted:

Name of On-Site Clinical Staff: _____

- Yes – Time of contact** _____
- No**

- N/A: Telephone interview**

Did participant desire contact information for counseling or other mental health treatment? **Yes** **No**

Was information provided? **Yes** **No**

Signature of Interviewer: _____ **Date:** _____

Check one:

_____ **Stage I Screening**

_____ **Stage II Telephone Interview**

_____ **Stage III 3-Month Follow-Up Interview**

Fax completed form to RTOG Headquarters (215-940-8830).

Reviewer 2:

1. Beyond documenting prevalence of depression in cancer patients using convenience samples, strategies to reduce the prevalence of untreated depressed cancer patients should be developed.

Response: This was not within the scope of the protocol.

2. The study samples were extremely homogeneous in ethnic and SES compositions.

Response: SES information was not collected on this study, but there were high proportions of patients who were white (83.3%) and not Hispanic or Latino (94.7%).

3. Impact of expected results was low. More scientifically rigorous research questions and study designs should be employed.

Response: There were fewer depressed patients than expected. It is hypothesized that the patients need to be screened closer to the time of diagnosis rather than closer to time of treatment.

Reviewer 3:

1. The objectives need to be better linked the study group. For example, if the objective was to focus on women with early breast cancer, then that should have been part of the objective.

Response: The breast cancer subset analysis was conducted post-hoc based on the large number of enrolled breast cancer patients.

2. One of the weaknesses is that the large number of patients was female, Caucasian. It doesn't seem to have been enough of a heterogeneous group of cancer patients. It would be helpful for the researchers to review this and make sure that their subjects represent the diversity of people with cancer.

Response: This is a major concern in clinical trial research and efforts are being undertaken to increase minority recruitment in clinical trials within NRG Oncology.

3. The authors note that they were interested in barriers to care. This might have been a vestige of the first set of objectives with the original design. It would be important, if the researchers are interested in barriers of care, to set the design in a more effective manner.

Response: Barriers to care was a secondary objective of this study.

4. It would be helpful to understand the statistics and determine if this study was powered appropriately, and whether a control group is needed.

Response: The main issue with the design of the study was due to the lower than expected rate of depression among this patient population.

5. In order to not have the IRBs turn down the project, it would be helpful for a clinician who has expertise in clinical issues, to review the protocol and make sure that patients with significant clinical problems such as major depression, hopelessness and suicidality, are seen in a timely manner and provided with care. Sometimes waiting room studies are workable, but sometimes they are not, and it would be helpful to understand these issues so that study design doesn't have to be so drastically modified.

Response: A secondary objective of this study was to collect information on how institutions offer care to patients with major depression, hopelessness and suicidality.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response:

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response:

Project Number: 0862404

Project Title: Assessment of Methods to Increase Latino Enrollment into
Cancer Clinical Trials

Investigator: Watkins-Bruner, Deborah

B. To ensure that feedback provided in the Final Performance Summary Report is utilized to improve ongoing and future research efforts, briefly describe your plans to address each specific weakness and recommendation as noted in Section B of the Final Performance Summary Report and listed below. If no weaknesses are listed below, no response is required.

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SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

I really enjoyed reading about this study. One recommendation is that the investigators provide the cultural training and the assessment tool to all researchers and practitioners and not limit access to members of RTOG.

Response: These tools are still being assessed for effectiveness but sharing publicly, once shown to be effective, can be considered.

Reviewer 2:

1. The sample size was inadequate to allow for definitive interpretation of the data. More people need to be included going forward.

Response: Agreed. More patients would have been ideal.

2. The types of trials appropriate for these tools should be discussed. Going forward this needs to at least be considered.

Response: The goal was to make the tools generic enough to be used in any clinical trial setting.

3. The materials developed through this research study should be provided for assessment.

Response: The assessment of the materials developed for this study is still being finalized.

Reviewer 3:

1. The project successfully met its objectives of developing patient education materials and investigator training programs and using cartographic modeling to perform a gap analysis. However, the primary objective of increasing Latino (and African-American) recruitment by 10% has yet to be assessed. I encourage the investigators to complete these analyses as they

will provide a test of the effectiveness of the Latino and African-American Cultural Competency and Recruitment Training Program.

Response: Minority accrual rates were computed pre-training and 3 months post-training by institutions with RAs who participated in the training and those with RAs who did not participate in the training.

Table 3.1
Minority Accrual

	Pre-Training	Post-Training	P-value [†]
Institutions with RAs who participated in the training	(n=46)	(n=46)	
Mean percent minority accrual	12.9%	14.4%	0.6411
Mean total accrual (std)	12.5 (14.6)	11.2 (11.7)	
95% Confidence Interval	(8.1, 16.8)	(7.7, 14.6)	
Mean total minority accrual (std)	1.9 (2.7)	1.7 (2.2)	
95% Confidence Interval	(1.1, 2.7)	(1.0, 2.3)	
Institutions with RAs who did not participate in the training	(n=401)	(n=401)	
Mean percent minority accrual	12.3%	12.6%	0.8837
Mean total accrual	5.4 (8.4)	4.6 (6.8)	
95% Confidence Interval	(4.5, 6.2)	(3.9, 5.3)	
Mean total minority accrual	0.9 (2.3)	0.8 (2.0)	
95% Confidence Interval	(0.6, 1.1)	(0.6, 1.0)	

Minorities included: black/African American, Hispanic/Latino and American Indian/Alaskan Native

[†] Paired T-test

2. The investigators planned to target 4 protocols to assess the impact of the educational materials and investigator training program. However, no list of the targeted protocols was provided. Such a list would provide more detail as to the disease sites that the investigators feel are more amenable to improvement in Latino and African-American recruitment.

Response: The investigators realized that targeting specific protocols would not yield enough data to determine the effectiveness of the training as not all of the institutions represented at the training participated in all of the targeted protocols. Since we collect minority accrual information on all of our trials, it was decided to examine the influence of the training across all trials participated in by each represented institution. Translated consent forms were provided for all of the group's Phase III studies.

3. It is unclear how the maps obtained using cartographic modeling will be used by RTOG to add sites with higher density Latino and African-American populations. A discussion of how the results will be used in the future would be helpful.

Response: GIS mapping has helped identify geographic patterns of overall and minority clinical trial accrual as well as high-density minority population areas without RTOG

member sites. This will help us strategically identify radiotherapy sites for outreach efforts as new partners in minority enriched locations to facilitate equal access to state-of-the-art cancer clinical trials. Mapping also identified high minority RTOG clinical trial accrual in lower minority dense sites that would not have been easily identified without mapping. This research is being readied for publication.

4. A statistical weakness is that the investigators state that they used a Wilcoxon-Mann-Whitney test to assess cultural diversity knowledge and attitudes of participants in the face-to-face RTOG training. This test assumes two independent samples. Since 42 of the participants completed surveys at baseline and follow-up, a more appropriate test is the Wilcoxon Rank-Sum test.

Response: Our apologies for this typo. The Wilcoxon Rank-Sum test and paired t-tests were used in the analysis of pre- and post-training scores.

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response: N/A

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):

Response:

Project Number: 0862407
Project Title: Quantitative Imaging Biomarker Tools
Investigator: Schnall, Mitchell

B. To ensure that feedback provided in the Final Performance Summary Report is utilized to improve ongoing and future research efforts, briefly describe your plans to address each specific weakness and recommendation as noted in Section B of the Final Performance Summary Report and listed below. If no weaknesses are listed below, no response is required.

(As you prepare your response please be aware that the Final Performance Summary Report, this Response Form, and the Final Progress Report will be made publicly available on the CURE Program's Web site.)

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

There is quality and reliability improvement due to the streamlining and integration of the different functions and processes and the generation of a report that can be viewed and exported to clinicians. It would be beneficial to the project if this impact is somehow quantified.

Response: We recently carried out a study to measure the impact of the ePAD tool on workflow, and we found a 15% improvement. (see Transl Oncol. Feb 2014; 7(1): 23–35.)

Reviewer 2:

1. Testing the software and technique development in this project for other imaging modalities (PET/CT, MRI) is desirable.

Response: This will be the subject of future work.

2. More readers and image cases should be included in future studies.

Response: We agree this would be good to pursue in the future.

3. Quantitative analysis of image before and after treatment should be thoroughly studied.

Response: We recently carried out a study to measure the impact of the ePAD tool on workflow, and we found a 15% improvement. (see Transl Oncol. Feb 2014; 7(1): 23–35.)

Reviewer 3:

1. Aim 3 needs additional data and more compelling data to support the efficiency of the approach. This concern is somewhat alleviated by the fact that the team is strong and the study analysis is ongoing.

Response: We recently carried out a study to measure the impact of the ePAD tool on workflow, and we found a 15% improvement. (see Transl Oncol. Feb 2014; 7(1): 23–35.)

2. There are no publications yet from this large effort. The analysis of the reader study needs to be completed and reported in a peer-reviewed journal.

Response: We recently published our work, see *Transl Oncol.* Feb 2014; 7(1): 23–35.)

C. If the research project received an “unfavorable” rating, please indicate the steps that you intend to take to address the criteria that the project failed to meet and to modify research project oversight so that future projects will not receive “unfavorable” ratings.

Response: not applicable

D. Additional comments in response to the Final Performance Review Report (OPTIONAL):