

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0828

Pilot Project To Reduce Missing RTOG Quality Of Life Data Via Electronic Web-Based Form Collection: A Companion Study For RTOG 0415 (A Phase III Randomized Study Of Hypofractionated 3D-CRT/IMRT Versus Conventionally Fractionated 3D-CRT/IMRT In Patients With Favorable-Risk Prostate Cancer)

Note: This is a limited institution trial open only to the institutions accruing to RTOG 0415 that are noted below. An additional 0.5 case credit will be obtained for each patient accrued to this study.

(6/22/09)

Akron City Hospital (Summa Health)	New Hanover Radiation Oncology Center
Albert Einstein Medical Center (Philadelphia)	North Shore
Duke University	Roswell Park Cancer Institute
Henry Ford Hospital	Saint Anne's Hospital (MA)
Kaiser Permanente	University of Utah
LDS Hospital	Veterans Affairs Medical Center (Long Beach, CA)
Main Line Health (Lankenau)	Washington University at St. Louis
Mayo Clinic	York Cancer Center
McMaster University (Hamilton, Ontario)	Zablocki VA Medical Center (Milwaukee)

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RTOG Headquarters 1-800-227-5463, ext. 4189

This protocol was designed and developed by the Radiation Therapy Oncology Group (RTOG) of the American College of Radiology (ACR). It is intended to be used only in conjunction with institution-specific IRB approval for study entry. No other use or reproduction is authorized by RTOG nor does RTOG assume any responsibility for unauthorized use of this protocol.

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Schema not necessary for this study. See **Section 11.0** for details regarding VisionTree Optimal Care.

Participating Institutions (6/22/09)

Akron City Hospital (Summa Health)
Albert Einstein Medical Center (Philadelphia)
Duke University
Henry Ford Hospital
Kaiser Permanente
LDS Hospital
Main Line Health (Lankenau)
Mayo Clinic
McMaster University (Hamilton, Ontario)
New Hanover Radiation Oncology Center
North Shore
Roswell Park Cancer Institute
Saint Anne's Hospital (MA)

University of Utah
Veterans Affairs Medical Center (Long Beach, CA)
Washington University at St. Louis
York Cancer Center
Zablocki VA Medical Center (Milwaukee)

Patient Population: (See Section 3.0 for Eligibility) RTOG 0828 is a limited institution trial open only to the above-noted institutions participating in RTOG 0415.

Only English-literate patients enrolled on RTOG 0415 who consented to participate in the quality of life component of that study (at one of these specified institutions) and have an e-mail address are eligible for enrollment in this companion study. (6/22/09)

Required Sample Size: 40 (6/22/09)

(Five patients will comprise the “run-in” portion of the companion study for sites to learn how to use the VisionTree software for electronic collection of the QOL data, followed by a maximum of 35 patients who will form the sample for the study analysis itself.)

1.0 INTRODUCTION

- 1.1 Missing data are a significant problem, particularly for quality of life (QOL) studies. Unlike data for traditional endpoints, such as survival, QOL data can never be obtained retrospectively if it is not provided by the patient at the appropriate time. This limits researchers' ability to accurately perform QOL statistical analyses and negatively impacts the clinical relevance of this effort.

Typically, QOL forms are filled out on "hard" copies (paper forms). To provide a more convenient method of filling out QOL information, the Radiation Therapy Oncology Group (RTOG) is working with a company, VisionTree Software, Inc (San Diego, CA), that will enable patients on this pilot study to fill out their QOL forms from any location that has a computer with Internet access. VisionTree has developed a new tool, VisionTree Optimal Care (VTOC), a HIPAA-secure, user-friendly, Web-based software system.¹⁻³ The VTOC tool contains a Web-based system for global patient and trial administration access, which allows improved compliance and accuracy of data collection, validation, and reporting. It is compliant with the Title 21, *Code of Federal Regulations*, Part 11 statistical process control system and provides a mobile solution for clinical trials. Outcomes data are collected with Microsoft Excel and PDF export of reports. VTOC also has mobile messaging and e-mail reminders. Surveys can be "pushed" to patients for completion at timed intervals (see <http://www.visiontree.com> for details). VisionTree has many clinical partners and clients, including ASTRO, University of California-San Francisco, Baylor College of Medicine, Duke University, Emory University, Harvard Medical School, Henry Ford Hospital, and University of Pennsylvania. ASTRO utilizes VisionTree outcomes on-line for maintenance of certification and capturing quality measures.

This technology would allow consenting patients to fill out their QOL forms on-line from any location and to receive e-mail reminders. E-mail reminders can also be sent to research associates at the appropriate institutions to remind them that a QOL time point window is about to close so that a patient can be contacted to fill out QOL information on time, before it becomes "missing."

The purpose of this companion study to RTOG 0415 is for RTOG to perform a pilot study to test the usefulness of this Web-based technology within the cooperative group mechanism. In particular, the goal of the pilot study will be to test the feasibility of the system and to see if it improves compliance of QOL data collection. Another goal of this study is to provide a more convenient way for patients to fill out their QOL information using the Internet (e.g., from home), thus, further improving collection of QOL data. The QOL data being collected in this study (and the time points at which they are collected) are exactly the same as in the QOL study described in protocol RTOG 0415. The key difference is that QOL information will be collected on a privacy-secure Web-based system which will be made available to patients through the Internet, using their e-mail addresses for identification and routine communication.

(6/22/09) The plan is to focus on the top accruing institutions within RTOG 0415 that agree to participate in this pilot study. As of April 6, 2008, 302 patients on RTOG 0415 have consented to participate in the QOL component of the study. RTOG 0415 randomizes patients to conventional intensity modulated radiation therapy (IMRT) versus hypofractionated IMRT for favorable-risk prostate cancer and has an overall accrual goal of 1067 patients. Of the 302 patients who consented to participate in the QOL component, more than 90% completed their baseline QOL forms [Expanded Prostate Index Composite (EPIC), EuroQol (EQ-5D), Hopkins Symptom Checklist (HSCL-25), and Utilization of Sexual Medications/Devices (SAQ)]. However, at the 6-month follow-up time point, the QOL form was overdue (by more than a 1-month window period) in approximately 50% of the patients. So far, 1-year QOL follow-up data are not available, but it is anticipated that the QOL completion rate will continue to decline over time. As has been noted across many QOL studies, there is a strong need to enhance QOL compliance, which is the overall goal of this pilot study. The primary goal is to determine if the implementation of the web-based VTOC system can improve the QOL completion rate at 6 months from 50% to 75%. The primary endpoint of the study focuses on the EPIC instrument, which is the main prostate QOL instrument in this study.

In the context of this study, the completion rate refers to completion of any part of the QOL form(s). In RTOG 0415, many of the QOL forms are only partially filled out. For example, at the 6 month follow-up time point, the following are the rates of returned QOL forms that were completely (100%) filled out: EPIC (64%), EQ-5D (96%), HSCL-25 (85%), and SAQ (41%). Moreover, 38% of the SAQ forms were missing up to 50% of the questions (compared to 1% of the other QOL forms). Similar findings were also noted at baseline. The reasons for this result are not entirely clear. While one possible explanation relates to the length of the instrument (e.g., the EQ-5D has only 5 questions), this may also relate to the sensitivity of the questions being asked (e.g., questions on the SAQ). The VisionTree Optimal Care (VTOC) software can provide a structure to further analyze this important issue, as it allows for real-time tracking, not only of how many patients completed particular forms, but also of the level of completeness of each form. VTOC can keep track if particular questions on a form are not routinely being answered. Patients can immediately be asked if they would like to answer the missing questions or not (to ensure that this was not due to an oversight). VisionTree can provide a rapid methodology to compare and contrast the level of completion rates between forms and determine precisely which questions are consistently not being answered.

Another interesting finding is that the most common reason provided for QOL forms not being completed at all was due to “institutional error” (ranging from 22-33% of the time at baseline to 32-41% of the time at the 6-month follow-up time point). An institutional error might be something as simple as the staff neglecting to provide patients with the QOL instruments. This finding, which becomes more prominent over time, provides further rationale for studying the VTOC software, as this methodology automatically gives patients the opportunity to access and fill out QOL forms from a secure web portal. It also allows for real-time monitoring of the QOL completion rates, thereby providing a potential method for intervention (e.g., via real-time reminders to both patients and research associates) to reduce missing QOL data.

Patients must have an e-mail address that they consent to use for the purpose of this study. Patients’ e-mail addresses are necessary for this study so that e-mail reminders may be sent to them to remind them to fill out QOL forms that are due. Patients who are interested in participating but do not yet have an e-mail address can obtain one for free from a number of sources (e.g., Yahoo!, Hotmail, or AOL) and thus, can still participate. The patient’s e-mail address will be used for password-protected access to VTOC. Patients can complete the QOL forms anywhere with a secure login. Patients will receive a login card (either printed or sent via e-mail) with which to log in using the secure, Web-based VTOC portal. VTOC meets all HIPAA guidelines and is encrypted (via 128-bit SSL) for the security, privacy, and confidentiality of QOL information. It is similar to the secure login commonly used when performing on-line banking. The login card can then be kept and maintained by the patient.

The patient’s e-mail address will only be used by RTOG for this study. Patients will only be sent e-mail reminders when QOL forms are due. A typical e-mail reminder would read: “Your Quality of Life forms for your study, RTOG 0828, are now due. Please go to <http://www.optimalcare.com> to use your secure login to log in to your portal and complete the on-line forms. If any questions make you feel uncomfortable, you may skip those questions and not give an answer. If you have any questions, please e-mail or call your research associate at [insert RA e-mail address] or [insert RA telephone number]. Thank you for participating in this study.” The reminders will be created by RTOG and placed into a study template that will be sent to patients at customized intervals (at the 5 time points when QOL forms are due). The first reminder will be sent at the beginning of the “window” to complete a QOL form, with a second reminder halfway through the window period if the QOL forms are not yet completed at that time. A maximum of 3 reminders will be sent for each of the 5 QOL time points; after a patient has completed all forms in the portal, a dialogue box will appear that says “Thank you for completing your Quality of Life forms,” and the patient will no longer receive any remaining notices for that time point. The site research associate or study administrator will be informed through the VTOC “At-A-Glance” form management system when QOL forms have been completed.

2.0 OBJECTIVES

2.1 Primary Objective

2.1.1 EPIC completion rate at 6 months. Completion rate is defined as completion of any part of the QOL forms.

2.2 Secondary Objectives

2.2.1 Completion rates for the SAQ, EQ-5D, and HSCL-25 at 6 months

2.2.2 Completion rates for the QOL forms (EPIC, EQ-5D, HSCL-25, and SAQ) at baseline, 12 and 24 months, and 5 years.

3.0 PATIENT SELECTION

NOTE: EXCEPTIONS TO ELIGIBILITY ARE NOT PERMITTED.

3.1 Conditions for Patient Eligibility

3.1.1 English-literate patients enrolled in RTOG 0415 who have consented to participate in the QOL component of this study are eligible. **Note:** Before patients are offered participation on the companion study, patients must have already consented to the QOL component of RTOG 0415. Patients who have consented to the QOL component of RTOG 0415 will be asked to respond to a brief questionnaire when they decline or accept participation in this companion study to help identify potential factors in their decision (see Appendix III).

3.1.2 Patients must have an e-mail address that they consent to use for the purpose of this study. Patients' e-mail addresses are necessary for this study so that e-mail reminders may be sent to them to remind them to fill out QOL forms that are due. Patients who are interested in participating but do not yet have an e-mail address can obtain one for free from a number of sources (e.g., Yahoo!, Hotmail, or AOL) and thus, can still participate. The patient's e-mail address will be used for password-protected access to VTOC.

3.1.3 Patients must be able to provide study-specific informed consent prior to study entry.

3.2 Conditions for Patient Ineligibility

3.2.1 Patients who declined to participate in the QOL component of RTOG 0415

3.2.2 Patients who do not read English

3.2.3 Patients who do not have an e-mail address that they consent to use for the purpose of this study. Patients who are interested in participating but do not yet have an e-mail address can obtain one for free from a number of sources (e.g., Yahoo!, Hotmail, or AOL) and thus, can still participate.

3.2.4 Patients without e-mail or Internet access are still able to participate in the QOL component of RTOG 0415 by choosing the traditional hard-copy (paper) method of forms completion. However, these patients would not be eligible for this pilot study.

4.0 PRETREATMENT EVALUATIONS/MANAGEMENT

Not applicable to this study

5.0 REGISTRATION PROCEDURES (11/4/08)

5.1 Patients who have consented to the QOL component of RTOG 0415 will be asked to respond to a brief questionnaire when they decline or accept participation in this companion study to help identify potential factors in their decision (see Appendix III). Institutions must submit this form to RTOG Headquarters within 1 week following patient acceptance or refusal to participate in the study (see Section 12.0). **Note:** Research associates will receive on-site training in VTOC by VisionTree personnel. Joint Centers that wish to participate in this study will receive their training from the member institution.

5.2 Patients will have been registered into RTOG 0415. An institution can enroll the patient into this companion study by faxing the questionnaire (Appendix III) to the RTOG Registration Desk at 215-574-0300.

6.0 RADIATION THERAPY

Not applicable to this study

7.0 DRUG THERAPY

Not applicable to this study

8.0 SURGERY

Not applicable to this study

9.0 OTHER THERAPY

Not applicable to this study

10.0 TISSUE/SPECIMEN SUBMISSION

Not applicable to this study

11.0 PATIENT ASSESSMENTS

Note: Research associates will receive on-site training in VTOC by VisionTree personnel. Joint Centers that wish to participate in this study will receive their training from the member institution.

- 11.1 Per the QOL component of the IRB-approved protocol RTOG 0415. This is a pilot companion protocol to RTOG 0415, assessing method and compliance of questionnaire completion. It does not add to or change the questionnaires from what is stated in 0415.
- 11.2 Patients must have an e-mail address that they consent to use for the purpose of this study. Patients' e-mail addresses are necessary for this study so that e-mail reminders may be sent to them to remind them to fill out QOL forms that are due. Patients who are interested in participating but do not yet have an e-mail address can obtain one for free from a number of sources (e.g., Yahoo!, Hotmail, or AOL) and thus, can still participate.
- 11.3 The patient's e-mail address will be used for password-protected access to VTOC. Patients can complete the QOL forms anywhere with a secure login. After enrollment on study, the research associate will give the patient a login card (either printed or sent via e-mail) with which to log in using the secure, Web-based VTOC portal. Research associates will receive on-site training by VisionTree regarding the preparation of login cards for each patient. VTOC meets all HIPAA guidelines and is encrypted (via 128-bit SSL) for the security, privacy, and confidentiality of QOL information. It is similar to the secure login commonly used when performing on-line banking. The login card will be kept and maintained by the patient. The patient's e-mail address will be used only by RTOG for the purpose of this study.
- 11.4 Patients will only be sent e-mail reminders when QOL forms are due. A typical e-mail reminder would read: "Your Quality of Life forms for your study, RTOG 0828, are now due. Please go to <http://www.optimalcare.com> to use your secure login to log in to your portal and complete the on-line forms. If any questions make you feel uncomfortable, you may skip those questions and not give an answer. If you have any questions, please e-mail or call your research associate (RA) at [insert RA e-mail address] or [insert RA telephone number]. Thank you for participating in this study."
- 11.5 The reminders will be created by RTOG and placed into a study template that will be sent to patients at customized intervals (at the 5 time points when QOL forms are due). The first reminder will be sent at the beginning of the window to complete a QOL form, with a second reminder halfway through the window period if the QOL forms are not yet completed at that time. A maximum of 3 reminders will be sent for each of the 5 QOL time points; after a patient has completed all forms in the portal, a dialogue box will appear that says "Thank you for completing your Quality of Life forms," and the patient will no longer receive any remaining notices for that time point. The site research associate or study administrator will be informed, through the VTOC "At-A-Glance" form management system, when QOL forms have been completed or when the window for forms completion has closed.
- 11.6 If the site RA receives notice that forms have NOT been completed, he or she will call the patient to remind the patient to fill out incomplete forms at that time or to inquire why forms have not been completed. The RA will complete the cover page for each form that was not completed, or if the patient completed hard copy forms rather than using VTOC, and submit the forms to RTOG Headquarters.
- 11.7 The EPIC, HSCL-25, the Utilization of Sexual Medications/Devices (SAQ), and EQ-5D will be collected at pretreatment (baseline) and at 6, 12, 24 months, and 5 years after RTOG protocol 0415 therapy starts. Patient self-assessment of symptoms will be performed using four primary

EPIC scales: urinary, bowel, sexual, and hormonal symptoms. The HSCL-25 has 25 items and is scored by a four-point likert scale (1-not at all, 2-a little, 3-quite a bit, and 4-extremely). A higher score means a worse mood or depression. The SAQ is designed to assess the use of erectile aids among patients treated for prostate cancer. This instrument is used to complement the sexual symptom domain in the EPIC. The EQ-5D is a two-part self-assessment questionnaire. The first part consists of five items covering five dimensions (mobility, self care, usual activities, pain/discomfort, and anxiety/depression). Each dimension is measured by a three-point likert scale (1-no problems, 2-moderate problems and 3-extreme problems). The second part is a visual analog scale (VAS) valuing the current health state measured by a 100-point scale with a 10-point interval. (0-worst imaginable health state, 100-best imaginable health state). We will transform the five-item index score and VAS score into a utility score between 0 (worst health state) and 1 (best health state) for comparative purposes.

12.0 DATA COLLECTION

Data should be submitted to:

**RTOG Headquarters*
1818 Market Street, Suite 1600
Philadelphia, PA 19103**

***If a data form is available for web entry, it must be submitted electronically.**

Patients will be identified by initials only (first middle last); if there is no middle initial, a hyphen will be used (first-last). Last names with apostrophes will be identified by the first letter of the last name.

12.1 Summary of Data Submission

<u>Item</u>	<u>Due</u>
Questionnaire (for patients on the QOL component of RTOG 0415 who either decline or accept participation in this companion study)—see Appendix III	Within 1 week after patient declines or accepts participation in this companion study
QOL forms cover sheets	Within 1 month of the QOL form being due. (Note: To be completed by the RA only if the patient did not complete a specific QOL form or if the patient completed a hard copy of the form.)

(**Note:** Electronic QOL forms will be kept on the VisionTree, Inc., Web site and transferred to RTOG headquarters.)

13.0 STATISTICAL CONSIDERATIONS

13.1 Study Endpoints

13.1.1 Primary

EPIC completion rate at 6 months

13.1.2 Secondary

13.1.2.1 Completion rate for the SAQ, EQ-5D, and HSCL-25 at 6 months

13.1.2.2 Completion rates for the EPIC, EQ-5D, HSCL-25, and SAQ at baseline, 12 and 24 months, and 5 years

13.2 Power Calculation and Sample Size (6/22/09)

See 13.2.1 for amendment to sample size.

The EPIC completion rate at 6 months for the QOL component of RTOG 0415 is 52%, which is based on the data available as of April 6, 2008, from patients already enrolled on RTOG 0415 who consented to the QOL component of this study (and whose 6-month QOL forms were already more than 1 month overdue). We expect that the completion rate of the EPIC at 6-months

(p) will improve by at least 25% in the cohort of patients participating in the QOL component using VTOC. The hypotheses are:

$$H_0: p \leq 0.52 \text{ vs. } H_A: p > 0.52$$

With the sample size, 60, 98% statistical power can be obtained using a one-sample proportions Z-test⁴ with a significance level of 0.025 (1-sided test) under the alternative hypothesis ($p=0.77$). Adjusting the number of cases for ineligible or un-analyzable cases by 15%, a maximum of 70 patients is required for this study. Because this is a pilot study, the plan includes a “run-in” time period for training the accruing sites involving a total of 30 patients (a maximum of 2 patients per site). We will accrue 100 patients including 30 patients in a run-in training period. After a site has accrued 2 patients, the next patient accrued to that site will count towards the analysis of the endpoints of this study.

We expect that the SAQ completion rate at 6 months will improve by at least 25% in the cohort of patients participating in the QOL component using VTOC from the completion rate of 50% in the cohort participating in the QOL component of RTOG 0415. With the sample size, 60, 98% statistical power can be obtained using a one-sample proportions Z- test⁴ with a significance level of 0.025 (1-sided test) under the alternative hypothesis ($p=0.75$). We also expect that the completion rate of the HSCL-25 and EQ-5D at 6 months will improve by at least 25% in the cohort of patients participating in the QOL component using VTOC from the completion rate of 51% in the cohort participating in the QOL component of RTOG 0415. With the sample size, 60, 98% statistical power can also be obtained using a one-sample proportions Z- test⁴ with a significance level of 0.025 (1-sided test) under the alternative hypothesis ($p=0.76$).

13.2.1 Amended Sample Size (6/22/09)

The accrual to 0415 is above the original expectation, and the study is projected to close sooner than anticipated. Also, the accrual for this pilot study is slower than expected. Hence, the original sample size for this study (100) may be too stringent to meet the requirement before 0415 closes to accrual. Additionally, since this is a pilot study, only a few samples should be necessary to assess adequate site training. The run-in sample will therefore be reduced from 30 patients to 5 patients.

The hypothesized ineligibility rate (15%) appears to be too strict as well. As of the few patients entered thus far, there is a high eligibility rate; the ineligibility rate is therefore reduced to 5%. Thus, the sample size will be adjusted based in part on these new developments. However, the hypotheses will remain the same, i.e.,

$$H_0: p \leq 0.52 \text{ vs. } H_A: p > 0.52,$$

with alternative $p=0.77$. The original power 98% was also extremely high and will be reduced to 85%. With this new power and a significance level 0.025, the one-sided Z-test for one-sample proportions yields a sample of size 33. Hence, with the new projected ineligibility rate of 5%, the sample required will be 35 patients. This number does not include the run-in sample of 5 patients. **Thus, total accrual will be 40 patients.**

With the new sample size 33, the power for each of the 6-month SAQ, HSCL-25, and EQ-5D completion rate objectives is now 85% , all other assumptions being the same for these secondary objectives as stated in the last paragraph of 13.2.

13.3 Patient Accrual (6/22/09)

See 13.3.1 for amendment to accrual.

Based upon patient accrual in previous RTOG prostate studies, there will be negligible accrual during the first 6 months while institutions are obtaining IRB approval. Patients must have already consented to the QOL component of RTOG 0415. Patients who have consented to the QOL component of RTOG 0415 will be asked to respond to a brief questionnaire when they decline or accept participation in this companion study, RTOG 0828, to help identify potential factors in their decision (see Appendix III). The average monthly accrual rate of RTOG 0415 is 24 patients. About 85% of the patients have been accrued from the top institutions and about 70% of the patients participate in the QOL portion of this study (as of April 6, 2008). We expect to accrue 6

patients per month for RTOG 0828, because we expect that 50% of the patients who participate in the QOL portion of the study will agree to use VTOC. With 6 patients per month, we expect to complete accrual in 23 months, including the first 6 months.

13.3.1 Amended Accrual (6/22/09)

Accrual to this pilot study is occurring according to projections in 13.3. However, due to the faster than projected accrual to 0415 and the impending closure (to accrual), the amended, reduced sample size should allow accrual completion for this pilot study prior to the closure of 0415.

13.4 Analysis Plan (6/22/09)

The completion rate for each QOL form (EPIC, EQ-5D, HSCL-25, and SAQ) is defined as the proportion of patients who complete any part of the QOL form at a specified time point (baseline, 6, 12, and 24 months, and 5 years) among patients who participate in the QOL portion of RTOG 0415 and agree to use VTOC. Completion is defined as completion of any part of the QOL forms. The QOL completion rate will be calculated at baseline, 6, 12, and 24 months, and 5 years for the four QOL forms. A one-sample proportions test⁴ will be done for each QOL form at each time point at the significance level of 0.025 at each time point.

Tabulation of patient's prior treatment, as well as the sociodemographic characteristics of patients who participate in this study will be reported. The frequency table for the following variables of interest will be reported: number of patients who consented to the QOL component of RTOG 0415, who have an e-mail address and agree to participate in this companion study, and the sociodemographic profile of patients likely to be interested in this type of methodology (i.e., using the Internet to complete QOL data forms).

The results of the VTOC QOL completion assessment will be useful to RTOG. If the VTOC web-based data collection strategy works, it will help reduce the problem of missing QOL data and will provide an important solution for future RTOG QOL studies.

13.5 Gender and Minorities (6/22/09)

13.5.1 Projected Distribution of Gender and Minorities

Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	N/A	1	1
Not Hispanic or Latino	N/A	39	39
Ethnic Category: Total of all subjects	N/A	40	40
Racial Category			
American Indian or Alaskan Native	N/A	<1	<1
Asian	N/A	1	1
Black or African American	N/A	6	6
Native Hawaiian or other Pacific Islander	N/A	<1	<1
White	N/A	33	33
Racial Category: Total of all subjects	N/A	40	40

REFERENCES

1. Gorgulho A, De Salles A, Mattozo C, et al. Definition of a Treatment Modality by the Patients Using a Decision-Making Software. Poster presented at: Annual Meeting of the American Association of Neurological Surgeons; April 18-20, 2005; San Francisco, CA.
2. Gorgulho A, De Salles A, Mattozo C, et al. VisionTree Software - Stereotactic Radiation vs. Conventional Surgery. Paper presented at: Annual Meeting of the International Stereotactic Radiosurgery Society; June 23-27, 2007; San Francisco, CA.
3. Pedroso A, De Salles A, Mattozo C, et al. Decision Support Software Use For Patients: Immediate and Post Evaluation. Paper presented at: Annual Meeting of the Congress of Neurological Surgeons; April 28-29, 2006; Los Angeles, CA.
4. Dixon, WJ and Massey, FJ. Introduction to Statistical Analysis (4th edition McGraw-Hill); 1983.

APPENDIX I

RTOG 0828

Informed Consent Template for Cancer Treatment Trials (English Language)

**Pilot Project to Reduce Missing RTOG Quality of Life Data
via Electronic Web-Based Form Collection: A Companion Study for RTOG 0415
(A Phase III Randomized Study of Hypofractionated 3D-CRT/IMRT Versus Conventionally Fractionated
3D-CRT/IMRT in Patients With Favorable-Risk Prostate Cancer)**

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You may also discuss it with your health care team. If you have any questions, you may ask your study doctor for more explanation.

You are being asked to take part in this study because you have agreed to participate in RTOG 0415 (and its quality of life [QOL] study). This is a companion study to test a new way to collect the QOL information, using the Internet.

Why is this study being done?

The purpose of this companion study is to test whether or not using the Internet (for example, using a computer in your home or at a local library) to fill out quality of life (QOL) forms is easier for patients. We want to find out whether or not a different way of filling out QOL forms (using a web-based system) will help patients fill out forms more completely and on time.

Typically, patients are asked to fill out QOL forms on paper. To test a different way of filling out QOL forms, the Radiation Therapy Oncology Group (RTOG) is working with a company, VisionTree Software, Inc, that has a Web site where patients can fill out QOL forms anywhere there is a computer with Internet access. The VisionTree Optimal Care (VTOC) site is secure. When you log in to the VTOC site, it will take you step-by-step through the process of filling out your forms. This study will help determine if the VTOC site is easy or difficult to use.

How many people will take part in the study? (6/22/09)

Approximately 40 patients at select institutions.

What will happen if I take part in this research study?

Before you begin the study ...

To participate in this study, you must be able to read English. You will need an e-mail address that you agree to use for this study. The e-mail address is needed to identify you on the VisionTree Optimal Care (VTOC) Web site and for e-mail reminders that will be sent to you when QOL forms are due. Your e-mail address will only be used by the RTOG for the purpose of this study, not for mail or telephone marketing purposes.

If you are interested in participating in this study but do not have an e-mail address, you may obtain one (quickly and for free at Web sites such as Yahoo!, Hotmail, or AOL) so that you can still participate. You can then complete the QOL forms at home or at any other computer with Internet access.

Your access to the VTOC Web site will be password-protected, and your e-mail address can be used to retrieve your VTOC password if you ever forget it or lose your login card. You will receive a login card either by regular mail or via e-mail with the information you will need to log in to the VTOC site for the first time. You will keep your own login card.

Whether or not you decide to participate in this companion study, you will be asked to fill out a brief questionnaire that will take about 5 minutes to complete and which is completely voluntary. This form asks questions regarding your experience with using computers, the Internet, and e-mail.

During the study ...

The QOL information we want to collect (and the time points at which it is collected) are exactly the same as the paper QOL forms used in the RTOG 0415 study, in which you have already consented to participate. The only difference is that QOL information will be collected on the VTOC Web site.

Instead of filling out paper forms, you will be asked to complete the same 4 forms at the same time points as in the main study (RTOG 0415), but on a computer with Internet access. You will use your e-mail address to access forms on the VTOC Web site and to receive reminders to fill out these forms. The 5 time points are: immediately before you enroll in the study, at 6, 12, and 24 months following the start of your radiation treatment, and at 5 years following the start of your radiation treatment. It takes about 25-30 minutes to fill out the forms.

You will only be sent e-mail reminders at the time that the QOL forms are due (a maximum of 3 e-mail reminders per QOL due date will be sent). A typical e-mail reminder would read as follows: "Your Quality of Life forms for your study, RTOG 0828, are now due. Please go to <http://www.optimalcare.com> to use your secure login to log in to your portal and complete the on-line forms. If any questions make you feel uncomfortable, you may skip those questions and not give an answer. If you have any questions, please e-mail or call your research associate at [*insert RA e-mail address*] or [*insert RA telephone number*]. Thank you for participating in this study."

The VisionTree Optimal Care (VTOC) Web site is a secure site. When you log in to the VTOC site, it will take you step-by-step through the process of filling out your forms. If you have not completed all forms after the 3 reminders, the research associate will call you to find out why you did not complete the form.

If any questions make you feel uncomfortable, you may skip those questions and not give an answer. The QOL questions ask about your view of how your life has been affected by cancer and its treatment. You will be asked how you are feeling physically and emotionally during your cancer treatment and how you are able to carry out your day-to-day activities.

How long will I be in the study?

You will be in this companion study for a total of 5 years.

Can I stop being in the study?

Yes. You may change your mind about completing the on-line forms at any time, and still remain in the QOL part of study RTOG 0415 by choosing to use hard (paper) copies of the forms to fill out your QOL forms. You may also stop being in the QOL study entirely.

The study doctor may stop you from taking part in this companion study at any time if he or she believes it is in your best interest to stop, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the pilot study?

You should talk to your study doctor about any questions or concerns that you have while taking part in this companion study.

Are there benefits to taking part in the study?

You may or may not benefit from participating in this study. A key goal of this companion study is to provide a more convenient way for you to fill out your QOL forms, using the Internet. We hope that the information from this study will help researchers improve the ability to collect such important QOL information in the future and help doctors better understand how patients feel during treatments and what effects the treatments have on patients. In the future, this information may help patients and doctors as they decide which treatments to use to treat cancer.

What other choices do I have if I do not take part in this study?

You may fill out your QOL forms for RTOG 0415 on paper forms provided to you by the research associate in the clinic or by mail. Talk to your study doctor about your choices before you decide whether you will take part in this companion study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Radiation Therapy Oncology Group (RTOG)
- The National Cancer Institute (NCI) and other government agencies involved in keeping research safe for people, like the Central Institutional Review Board (CIRB) and the Food and Drug Administration (FDA)
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute to provide greater access to cancer trials [for CTSU participants only]
- A Data Monitoring Committee (DMC) that regularly meets to monitor safety and other data related to this study
- VisionTree Software, Inc.

What are the costs of taking part in this study?

You will not be paid for taking part in this study. To fill out the QOL forms on-line, you will need access to a computer with Internet capability. This computer/Internet access will not be provided to you on this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://www.cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" resource guide from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy of the resource guide.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care or your participation in the main study, RTOG 0415. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number].

For answers to questions about your rights while taking part in this study, call the _____ [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at _____ [telephone number]. [Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]

You will get a copy of this form. If you want more information about this study, ask your study doctor.

Signature

I have been given a copy of all _____ [insert total of number of pages] pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant _____

Date _____

APPENDIX II

STUDY PARAMETER TABLE

	Baseline (at enrollment)	Follow-Up (6, 12, and 24 months and 5 years following the start of RT)			
EPIC (PF)	X	X	X	X	X
EQ-5D (QL)	X	X	X	X	X
HSCL-25 (PQ)	X	X	X	X	X
SAQ (SB)	X	X	X	X	X

Institutions: PLACE LABEL FROM RTOG 0415 HERE

APPENDIX III (11/4/08)

Questionnaire for Patients Declining or Accepting Participation in the Companion Study

1. Do you have a computer at your home? Yes / No
2. Do you use a computer outside of your home? Yes / No
3. If Yes, where? Work/Library/School/Community Center/Other _____
4. Do you use the Internet (World Wide Web)? Yes / No
5. If Yes, about how often? Once per..... Day/Week/Month/Other _____
6. If Yes, do you ever fill out forms or order things on the Internet? Yes / No
7. Do you have an e-mail address? Yes / No
8. If Yes, about how often do you use e-mail? Once per..... Day/Week/Month/Other _____
9. Are you currently retired? Yes / No
10. What is or has been your main occupation? _____
11. Please share with us any other comments or suggestions.
