

AD _____

Award Number: W81XWH-08-2-0174

TITLE: Targeted Radiation Therapy for Cancer Initiative

PRINCIPAL INVESTIGATOR: John Halligan, MD

CONTRACTING ORGANIZATION: The Geneva Foundation
Lakewood, WA 98496

REPORT DATE: September 2010

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

Approved for public release; distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE (DD-MM-YYYY) 01-09-2010	2. REPORT TYPE Annual	3. DATES COVERED (From - To) 4 AUG 2009-3 AUG 2010
--	---------------------------------	--

4. TITLE AND SUBTITLE Targeted Radiation Therapy for Cancer Initiative	5a. CONTRACT NUMBER
	5b. GRANT NUMBER W81XWH-08-2-0174
	5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S) Stephanie Ninneman, CRM, Michael Brown, MD john.halligan@providence.org	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) The Geneva Foundation Lakewood, WA 98496	8. PERFORMING ORGANIZATION REPORT NUMBER
--	---

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) US Army MPMC Fort Detrick, MD 21702-5012	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public distribution; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
This program is intended to establish the infrastructure to provide state-of-the art targeted radiation therapy to military personnel and veterans with cancer. The research aspect of this project is intended to demonstrate whether

- 1) targeted radiation therapy with real time localization and tracking will allow use of a smaller planning treatment volume margin with a significant decrease in rectal and bladder volume treated and whether the use of such targeted therapy can occur within standard treatment times and thus feasible for routine clinical use,
- 2) whether the use of Vac-Lok® immobilization devices are necessary when patients are treated using the Calypso system,
- 3) whether Beacon® Transponder is of benefit in pelvic radiation therapy following prostatectomy,
- 4) whether hypofractionated treatment plans which are more beam on time per fraction which may potentially account for more intra-fraction organ movement but allow for a shorter duration of treatment are feasible for routine clinical use with the Calypso system and
- 5) whether the localization of external beam radiation therapy (EBRT) can be improved to cancers of the liver.

15. SUBJECT TERMS
Calypso, Prostate, Intensity Modulated Radiation Therapy (IMRT), Planning Target Volume (PTV), Beacon Transponders

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 9	19a. NAME OF RESPONSIBLE PERSON USAMPMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	5
Problem Areas.....	8
Key Personnel Updates.....	8
Key Research Accomplishments.....	8
Reportable Outcomes.....	9
Conclusion.....	9
References.....	9
Appendices.....	9

Targeted Radiation Therapy for Cancer Initiative Annual Report

Introduction:

The full potential of radiation therapy has not been realized due to the inability to locate and track the tumor target continuously during the delivery of the radiation dose. Without the ability to accurately locate the tumor target at the time of dose delivery, more of the patient's healthy tissue is exposed to radiation, which may result in acute or chronic complications. The research studies and activities described will improve the techniques of modern radiation therapy and directly benefit the Departments of Defense and Veterans Affairs by: providing improved, state-of-the-art prostate cancer treatments to active-duty military personnel and veterans; continuing to investigate reduction of the number of daily radiation treatments required for each patient thereby reducing the cost of care and increasing treatment capacity within the military and veterans health care delivery system; enabling research to establish standards of care for targeted radiation therapy; establishing a DOD center of excellence in targeted radiation therapy and accelerating the development of the targeted radiation therapy platform to treat additional cancers that significantly affect service personnel and veterans, such as nonresectable cancers of the liver. The Calypso® 4D Localization System is utilized to track both inter-fraction and intra-fraction tumor movement in patients receiving radiation therapy for various malignancies. Improved tracking of tumors may lead to improved therapeutic outcomes. The Calypso® 4D Localization System is a FDA Class II device.

Body: Task Completion

Task 1. *Establishment of centers for targeted radiation therapy at MAMC and VAPSHCS with installation of the Calypso® 4D Localization System.*

- Installation of the Calypso® 4D Localization System has successfully occurred at both MAMC and VAPSHCS.
- The radiation team at MAMC has continues to receive training and technical support of the system from Calypso as needed, including most recently, prostate bed beacon implant training provided to the urologists in April. The trainers from Calypso brought a demonstration DVD and provided support during the implantation of three (3) prostate bed patients enrolled on the post-prostatectomy protocol.
- As stated in Year 2 Quarter 3 progress report, there has been a delay with training for the VAPSHCS team. Prior to any training occurring, the QA process to commission the system has to occur. There were significant delays in the process to contract this commissioning service out. On 17 June 2010, The Geneva Foundation sent a letter to VAPSHCS providing notice that the IMRT commissioning had to be scheduled and evidence of active recruitment provided by 3 August 2010 or The Geneva Foundation would remove the localization system and identify a new research site. On 3 August 2010, VAPSHCS provided The Geneva Foundation notice that a contract would be fully executed with a physicist by the end of the week and that IMRT commissioning would be scheduled soon after. VAPSHCS has provided notice that the commissioning process started on 27 August 2010 and an eligible patient has been identified to begin treatment.

Task 2. *Treatment for prostate cancer with state-of-the art technology to allow real-time localization and continuous tracking of the tumor target.*

- A total of 12 non-study patients who did not otherwise qualify for a protocol have been treated with the Calypso system. Non-protocol patients have allowed the providers to gain further proficiency with the Calypso unit. We recently treated a patient with a very large abdomen (beyond the constraints of the allowed anatomical measurement to localize and track using the Calypso system) in the prone position rather than the established supine position. With the gained experience and success of treating this patient off protocol, we amended the Reduced PTV Margins protocol to allow for subjects to be placed in this alternate position if needed.
- VAPSHCS will also treat non-protocol patients simultaneously with protocol patients to gain expertise. The VAPSHCS has identified a non-protocol patient to begin treatment upon completion of IMRT commissioning.

Task 3. *Feasibility study with reduced planning treatment volume (PTV) margins and intensity modulated radiation therapy (IMRT) using targeted radiation therapy.*

- In the last year, 6 new subjects have been enrolled in the study with Reduced PTV Margins at MAMC. A total of 8 have been enrolled to date; 2 are in the treatment phase and 6 are in the follow-up phase. Three amendments received MAMC IRB approval including: 1. Dr. Macdonald was added as an associate investigator. 2. Protocol status changed to multicenter by adding VAPSHCS as well as some minor administrative changes. 3. Prone positioning was added as an alternate positioning method. Continuing review for the protocol was approved by the MAMC IRB and granted from 21 July 2010 through 20 July 2011.
- VAPSHCS is administratively ready to commence enrollment in this protocol, however, as stated in task 1, this cannot happen until IMRT has been commissioned. The VA team is optimistic that they will be able to identify and enroll a study patient promptly after the commissioning and training have been completed. VAPSHCS is also optimistic that they will have a large patient population that meet the criteria for enrollment.

This study is expected to enroll a combined total of 40 subjects from both centers.

Task 4. *A Hypofractionated IMRT Therapy in Patients with Favorable Risk Prostate Cancer Using the Calypso® 4D Localization System: A Feasibility Study.*

We are awaiting the preliminary results from the RTOG 0415, which is a similar hypofractionated study (not using the Calypso System), to verify safety prior to proceeding with drafting the protocol manuscript. If the RTOG trial proves to have negative outcomes, it would be clinically irresponsible to move forward with this protocol, and this task would need to be re-evaluated. Enrollment on this study closed 11 December 2009. We anticipate preliminary data to be released at the upcoming ASTRO conference being held the first week of November 2010.

This study is expected to enroll a combined total of 20 subjects from both centers.

Task 5. *A Randomized Study Comparing External Pelvic Immobilization to Limited Immobilization for the Treatment of Prostate Cancer with IMRT Using Real-Time, State-of-the-Art Motion Tracking with the Calypso® 4D Localization System.*

- IRB approval for this protocol at MAMC was granted on 24 November 2009 and one amendment adding Dr. Macdonald has occurred since. Three subjects have consented for trial; 1 completed treatment and is in the follow-up phase, 1 withdrew consent (decided to get proton therapy) and 1 will start treatment in the next week or so.

- VAPSHCS is in the process of submitting this protocol for regulatory review. It is anticipated that the protocol will be reviewed October 2010.

This study is expected to enroll a combined total of 20 subjects from both centers.

Task 6. *Post-prostatectomy Daily Target Guided Radiotherapy Using Real-Time, State-of-the-Art Motion Tracking with the Calypso® 4D Localization System: A Feasibility Study.*

- IRB approval for this protocol at MAMC was granted on 05 March 2010 and one amendment adding Dr. Macdonald has occurred since. Five subjects have consented for trial; 4 completed treatment and are now in the follow-up phase and 1 withdrew consent (decided to stay on active surveillance).
- VAPSHCS is in the process of submitting this protocol for regulatory review. It is anticipated that the protocol will be reviewed October 2010.

This study is expected to enroll a combined total of 10 subjects from both centers.

Task 7. *Phase I/II trial of Real Time targeting of metastatic lesions in the liver with hypofractionated radiation therapy.*

- The protocol manuscript has not yet been written.

This study is expected to enroll a combined total of 20 patients from both centers.

Task 8. *Establish a center of excellence for targeted radiation therapy.*

- Our site was recently acknowledged in two print articles which ran in the Ranger (a local newspaper that targets military retirees) and the Mountaineer (a paper that is distributed within MAMC and also to retirees and active duty). The articles included our growth and efficiency of the multidisciplinary prostate cancer clinic as well as our affiliation with research and the Calypso System,
- We plan on hosting an educational conference in the area of urology and radiation oncology focusing on current evidence based approaches for hormone therapy for the management of prostate cancer. We have coordinated with the department of urology and invited Dr. Christopher Amling, a urologist from Oregon Health and Science University as the key note speaker. The event is scheduled to take place on 01 October 2010. We believe this will promote our site as a “center of excellence in target radiation therapy” and encourage physicians in the community to seek our expertise.

- We are collecting information regarding problems/challenges encountered with Calypso as a “Lessons Learned Log” which identifies the problems encountered with possible causes and the techniques used to solve the problem.

Task 9: *Present findings of feasibility studies at professional conference.*

- We anticipate presenting the initial findings of the feasibility studies at ASTRO (American Society for Therapeutic Radiation Oncology) beginning in 2011.

Problem Areas:

- Delay in getting VAPSHCS site up and running due to lack of IMRT commissioning support. As stated prior in this report, a contract physicist has now been hired and has begun the commissioning process as of 27 August 2010. They will now receive the final training needed to begin using Calypso, and in fact, have already identified a patient to be treated. We recognize that this has been an issue with the progress of this research study and will continue to monitor and will promptly update the sponsor regarding any changes to status.
- It was anticipated that the protocol for the liver study would be written and would be under review in preparation to be submitted to MAMC IRB. There has been a delay in this task as the author of this protocol has had scheduling conflicts and has not been able to begin this task. A revised timeline for this protocol will be developed and an update will be provided to the sponsor regarding this new timeline.

Key Personnel Updates:

- Dr. Dusten Macdonald, associate investigator at MAMC has been deployed to Kuwait for 6 months. We anticipate his return to the clinic to be mid-to-late January 2011.
- Dr. Brent Tinnel joined the MAMC Radiation Oncology team in July 2010 and has recently been added to the Reduced PTV Margins and Post-prostatectomy protocols. He will also be added to the Immobilization protocol as soon as we receive continuing review approval.

Key Research Accomplishments:

- Enrolled 8 subjects on the Reduced PTV Margins protocol
- Enrolled 2 subjects on the Immobilization protocol

- Enrolled 4 subjects on the Post-prostatectomy protocol
- Treated 12 non-study patients with Calypso
- Completed a rough draft paper on the subject of fecal continence, supported by patient data from the Reduced PTV Margins protocol. Paper title: “Small Reductions in Planned Treatment Volumes Can Produce Notable Reductions in Radiation Dose To Healthy Tissues.”

Reportable Outcomes: None at this time.

Conclusion: None at this time.

References: N/A

Appendices: N/A