



DEPARTMENT OF VETERANS AFFAIRS
Veterans Health Administration
National Health Physics Program
2200 Fort Roots Drive
North Little Rock, AR 72114

OCT 16 2008

In Reply Refer To: 598/115HP/NLR

Cassandra F. Frazier
Division of Nuclear Material Safety
U.S. Nuclear Regulatory Commission, Region III
2443 Warrenville Road, Suite 210
Lisle, Illinois 60532-4352

Re: NRC License 03-23853-01VA

Dear Ms. Frazier,

I am forwarding the enclosed report regarding NRC Event Number 44219. The report addresses 36 medical events that occurred at the VA Medical Center, Philadelphia, Pennsylvania, and is submitted pursuant to 10 CFR 35.3045(d). The medical center holds VHA Permit Number 37-00062-07 under our master material license.

Please note that 37 medical events were reported to the NRC Operations Center on October 2, 2008. The events involved permanent implant prostate seed brachytherapy. Upon re-evaluation, only 36 medical events occurred. We are currently reviewing their methodology for dose assessment for these events, which mainly involved extra-prostatic seeds.

My staff performed the initial on-site part of a reactive inspection May 28-29, 2008, and returned June 24-25, 2008, to evaluate the circumstances of related events, assess initial actions to prevent a recurrence, and assess regulatory compliance. At the exit meeting on May 29, 2008, the inspectors asked the medical center to review a sample of additional brachytherapy treatments. This ongoing review by the medical center revealed additional patient procedures that meet the definition of a medical event. The NRC Operations Center was notified of these additional medical events on June 6, 12, 21, 25; July 2, 8, 10, 15, 18, 22, 25; August 6, 13, 22; and on October 2, 2008. The additional events were recorded by the NRC Operations Center as updates to Event Number 44219. This report addresses the additional medical events reported to NRC on October 2, 2008.

If you have any questions, please contact me at (501) 257-1571.

Sincerely,


E. Lynn McGuire
Director, National Health Physics Program

Enclosure

Possible Medical Event NRC Event No. 44219 – Phase 2

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1) Rectum (continued)

b) Patients with dose to rectum >150% of planned with Dose < 160 Gy = 7

Patient XRT #	Implant Date	%	Dose Gray	Number of External Seeds		
				>1 cm	Perineum	Bladder
067	7-2-07	223%	106	6	5	1
053	1-10-05	172.8%	143.9	8	4	0
048	10-15-07	208.5%	158	8	3	1
114	7-24-06	184.7%	140.5	8	2	Not visible
111	4-23-07	176.8%	128.6	9	7	0
022	7-22-02	214%	122	0	0	5
049	3-27-04	157.8	106	5	4	1

2) Seeds External to the Prostate Circumference at Distance(s) Greater than 1 cm from Prostate Surface

a) External Seeds Primarily Not in Perineum >1cm = 5

Patient XRT #	Implant Date	Rectal Dose Gray	Number of Seeds		
			>1 cm	Perineum	Bladder
041	6-5-06	93.2	6	5	0
074	3-10-07	101	10	4	0
021	6-13-05	134.6	9	0	0
028	11-25-02	46	8	0	0
024	1-3-05	100	10	1	0

b) External and Inferior to Prostate (In Perineum) = 9

Patient XRT #	Implant Date	Rectal Dose Gray	Number of Seeds		
			>1 cm	Perineum	Bladder
030	2-6-06	94.8	8	6	1
026	10-18-04	110.2	13	8	2
095	7-21-03	58	9	7	0
012	7-11-05	120	9	8	0
019	8-30-04	129.4	20	20	0
088	5-15-06	114.7	20	11	0
094	1-14-08	108.6	7	7	1
015	11-1-04	62.9	9	9	1
089	10-21-02	128.4	9	8	

3) Bladder = 6

Patient XRT #	Implant Date	Rectal Dose Gray	Number of Seeds		
			>1 cm	Perineum	Bladder
004	2-14-05	86	4	3	3
073	11-4-02	56.5	6	0	3
071	11-15-04	104	17	11	3
009	12-6-04	94	17	6	9
042	9-8-03	101.7	20	20	12
*011	10-3-05	112.9	20	20	6

* [D90<80% - 2005 Non-Med Event]

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4) Deceased Patients - Both had D90<80%

Patient XRT #	Implant Date	Rectal Dose Gray	Number of Seeds		
			>1 cm	Perineum	Bladder
003	6-20-05	73.9	7	4	1
112	4-19-04	75.8	0	0	0

Phase I – Identification of Prostate Dose Deviation of 20% or more

Previous reports of Possible Medical Events were submitted in compliance with 10CFR 3045 (a) (1) and (i):

(a) A licensee shall report any event, except for an event that results from patient intervention, in which the administration of byproduct material or radiation from byproduct material results in—

(1) A dose that differs from the prescribed dose or dose that would have resulted from the prescribed dosage by more than 0.05 Sv (5 rem) effective dose equivalent, 0.5 Sv (50 rem) to an organ or tissue, or 0.5 Sv (50 rem) shallow dose equivalent to the skin; and

(i) The total dose delivered differs from the prescribed dose by 20% or more

Records for 114 procedures for 112 patients were reviewed. Patients with post-treatment plans with D90 dose to the prostates less than 80% of the dose specified in the Written Directive were identified and requested to obtain a recent CT scan in order to allow re-contouring and recalculation of prostate doses. Of this group, 55 brachytherapy procedures were found in which the administered dose to the prostate may have differed from the prescribed dose by more than 0.5 gray and the total dose delivered may have differed from the prescribed dose by 20% or more. These possible medical events were reported to the VA National Health Physics Program, who in turn reported them to the Nuclear Regulatory Commission in compliance with the reporting requirements stipulated in 10 CFR 35.3045.

Phase II Identification of Dose(s) External to the Prostate

This report is provided in accordance with 10 CFR Part 35.3045

Report and notification of a medical event.

(3) A dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) to an organ or tissue and 50% or more of the dose expected from the administration defined in the written directive (excluding, for permanent implants, seeds that were implanted in the correct site but migrated outside the treatment site).

As part of the review process, initial post-treatment plans that showed D90 prostate doses greater than 80% of the prescribed dose were reviewed by an external expert radiation oncologist. For any contours that he felt should be revised, the patient(s) were contacted and requested to obtain a recent CT. This CT was then contoured and an independent radiation therapy medical physicist recalculated the prostate dose as well as dose to the bladder and rectum. For those original post-treatment CT scans with contours deemed acceptable, the number and location of seeds were evaluated and recalculated by the consultant radiation therapy medical physicist.

Criteria used to identify dose to organ or tissue other than the prostate:

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The tissue and organs external to the Prostate that were evaluated are Rectum, Tissue external to the prostate including the perineum and Bladder wall.

Rectum – Dose to 1.33cc volume exceeded 150% of the Pre-treatment plan dose

External Tissue including Perineum –
5 or more seeds located beyond 1-cm exterior, and inferior, to the surface of the prostate

Bladder - 3 or more seeds located in the bladder wall.

Basis for criteria

With 160 Gray as the prescribed prostate dose, the expected dose to the rectum and bladder would be 160Gray because of the close proximity of these organs to the prostate. However, dose varies greatly with volume specified. No pre-treatment volumes for organs or tissue outside the prostate were documented.

Rectum

D1.33 is the dose to 1.33 cc . It was chosen because it is the volume the Variseed treatment planning program uses to identify high dose volume during pre-planning.

It is also a value found in the literature:

“Defining the Risk of Developing Grade 2 Proctitis Following I-125 Prostate Brachytherapy using a Rectal Dose-Volume Histogram Analysis” K. M. Snyder, M.D., et al, Int. J. Rad. Oncology Bio. Phys. Vol. 50, No.2,pp 335-341, 2001

Pre- treatment and post-treatment Doses to 1.33 cc volume were compared to determine the “expected dose”. If the dose to 1.333 cc equaled or exceeded 150% of the expected dose, it was considered to be a medical event. If the dose to this volume exceeds 160Gy, it is considered to be clinically significant.

Tissue External to Prostate

A 1 cm perimeter was chosen since it fully encompassed seeds positioned parallel and perpendicular to the external prostate surface. Any seed protruding beyond the 1 cm cloud around the prostate was counted as exterior to the prostate and evaluated for clinical relevance and for dose contribution to the perineum, rectum and bladder.

Tissue Inferior to Prostate

The criteria of number seeds in tissue external to the prostate was refined to address unexpected dose to the perineum. The number of seeds located inferiorly at greater than 1 cm beyond the external surface of the prostate that approximated 10%, or more, of the total number of seeds implanted.

This approach was chosen since NRC defines dose as the product of the number of sources multiplied by activity multiplied by implant time. Since these are permanent implants, the number of seeds multiplied by activity was chosen as a conservative criteria to ensure we captured all procedures that may be deemed a medical event.

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The minimum number of total seeds implanted in any of the patients in Phase 2 was 53 seeds. Using 10% of this number, 5 or more seeds located more than 1-cm exterior to and inferior to the surface of the prostate was selected as the trigger level criteria for possible medical event. This number was chosen regardless of whether seeds were grouped versus dispersed. While seeds that are grouped together would yield a greater total dose to a particular region or tissue, seeds dispersed through a larger area may not produce as significant damage although this cannot be ruled out.

Bladder

Pre-treatment plans did not include the bladder since the plans were based on ultrasound images. Therefore, the post-treatment plan could not be compared to the pre-treatment plan to generate the expected bladder dose.

The 3-seed criteria was chosen after reviewing one patient's plan which showed that 2 seeds in the bladder wall contributed less than 60Gy to the bladder wall. The dose to the bladder wall with the seeds in the wall was compared to the bladder wall dose with the seeds removed. This is well below the bladder tolerance dose. However, additional evaluations using the Variseed isodose "cloud" showed the dose to tissue varied widely (106 to 240 Gy) depending on the dose-cloud selected surrounding the seed. Varian was contacted for information about how to determine the tissue volume within the dose cloud. This information will be used to re-evaluate bladder wall dose.

Summary of Findings:**a) The following patients had prostate D90's >80%**

1) **Rectum** – 14 patients were found to have received a dose to 1.33 cc volume greater than 150% of the expected. Seven patients had doses greater than 160Gy to the rectum and 7 had less than 160Gy. Rectal doses less than 160 Gray are not considered clinically significant.

Note: One of the patients with rectal dose >160Gy was the 2003 patient whose first implant was determined not to be a medical event. The rectal dose listed is from 2 implants.

2) Tissue External to Prostate

Close to Prostate – 6 patients have 5, or more, seeds located beyond 1-cm volume circumference. One of the deceased patients is included in this group

Perineum -9 patients have 5 or more seeds at more than 1-cm external and inferior to prostate

3) **Bladder** - 5 patients had 3 or more seeds in their bladder walls.

b) Deceased Patients = 2

While these patients have a prostate D90 <80%, they are being reported to ensure transparency and completeness. One of the two deceased patients had more than 5 seeds external to, but not inferior to, the prostate.

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Description of the Event:

Permanent prostate brachytherapy implant procedures were performed using Iodine-125 seeds on the dates listed above. The activity per seed and number of seeds prescribed in the written directives and used in the original treatment plans were ordered, received and implanted. The original post-treatment plans for the above patients were based on CT scans obtained the day after the Implant Date.

Initial post-treatment plans that showed D90 prostate doses greater than 80% of the prescribed dose were reviewed by an external expert radiation oncologist. For any contours that he felt should be revised, the patient(s) were contacted and requested to obtain a recent CT. This recent CT was then contoured and an independent radiation therapy medical physicist recalculated the prostate dose as well as dose to the bladder and rectum. For those original post-treatment CT scans with contours deemed acceptable, the number and location of seeds were evaluated and recalculated by the consultant radiation therapy medical physicist.

The D90 prostate doses for 33 of the above 36 patients were greater than 80% of the planned prostate dose. The other 3 patients with D90 less than 80% of the planned dose are included for completeness and include the two patients who have passed away in the intervening time since their brachytherapy procedure. Neither death was deemed related to the brachytherapy procedure or any complication related to the procedure. Both were reported in prior communications with the NRC. The third patient is one reported to NRC in 2003 and was the subject of a special Investigation by the NRC in 2003. This patient and procedure was deemed not to be a medical event.

On October 1, 2008, the RSO and Chief of Radiation Oncology Service completed their review of the results for the above patients and determined Medical Events had occurred. On October 1, 2008, the RSO notified NHPP of these findings. The data for these patients is being reviewed as part of the causal analysis currently in process. Any necessary procedural changes will be implemented to prevent a recurrence before any additional brachytherapy procedures are performed. The brachytherapy program was formally put on-hold in early June, 2008 and remains on-hold.

Why the Event Occurred:

Causal analysis is a charge to the Administrative Board of Investigation (ABOI) that is in process. All external review has been subsumed by and into the ABOI per the PVAMC Director. Final recommendations and completion of the review of the Internal Review Team are pending review of other bodies.

Preliminary observations by the Internal Review Team that require validation and further input include the following:

- Lack of proper local Quality Control and Management of brachytherapy program
- Lack of policies to address post-implant management of patients and patient dosing
- Interruption of connectivity between radiation oncology and radiology for a period of approximately 1 year: This contributed to the inability to calculate patient doses during this time frame, but it was not causative for doses being outside of accepted range
- Lack of program oversight with inadequate review surrounding past trigger events relating in part to lack of policies to address programmatic review

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One possible cause that was eliminated was the possible incorrect conversion of millicurie to the “U” factor. That conversion was verified as correct.

Effect on Patient:

Effect on patients is still under review. Patients are being followed using established medical criteria (e.g. PSA) to evaluate possible effects of under-dosing which could include treatment failure. If it appears treatment failure is occurring, patient records are being reviewed by independent experts to obtain possible treatment options which will be offered to the patient. Each case is being individually reviewed to determine if additional treatment is indicated and what specific modality would be most efficacious with respect to clinical condition, PSA levels and initial dosing. Recent phone calls to patients are providing updated information on their condition. Appropriate clinical support is being provided as needed.

Corrective Actions:

1. Program was placed on-hold in early June, 2008 and remains in that status pending results of on-going investigation.
2. Institution of local QC/QM program in Radiation Oncology was established as of July 27 and is on-going.
3. In July 2008, Radiation Safety Committee initiated requirement for, and review of, QC programs in Nuclear Medicine, Radiology, Dental and Cardiology in addition to Radiation Oncology.
4. Complete policy review of brachytherapy and development of new policies to address pre and post-implant care; final recommendations are pending the outcome of on-going investigation.
5. Training for VA and Affiliated University Radiation Oncology staff in radiation safety procedures, and in particular the definition and recognition of a medical event and PVAMC Open Door Policy, has been completed for current personnel but is instituted as an ongoing process. Re-training Nuclear Medicine staff and Radiation Safety Committee members about Medical Events has been implemented.
6. Review of procedure to determine the optimal timing of post-implant CT scans (1 day versus 30 day) and to determine the logistics in obtaining such CT scans. Final process policies will be instituted based on the format of brachytherapy in the future as to whether this program will be either “real-time” or whether implants will be performed in the OR as per present protocol.

Patient and physician notification:

The referring physician and patients detailed in this report have been notified in compliance with 10 CFR 35.3045. Patients with new medical events related to radiation dose to organs and tissues external to the prostate gland were informed of the reason for notification.