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**NRC/INEL Radiation Therapy
Misadministration Investigation
Team Report 9402**

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Acronyms

| | |
|------|---------------------------------------|
| CFR | Code of Federal Regulations |
| cGy | centigray |
| Gy | Gray |
| INEL | Idaho National Engineering Laboratory |
| mCi | millicurie |
| mR | millirem |
| NMT | nuclear medicine technologist |
| NRC | Nuclear Regulatory Commission |
| PTD | Peripheral Tumor Dose |
| QA | Quality Assurance |
| QM | Quality Management |
| QMP | Quality Management Program |
| RSC | Radiation Safety Committee |
| RSO | Radiation Safety Officer |

NRC/INEL Radiation Therapy Misadministration Investigation Team Report 9402

Introduction

Purpose

The Nuclear Regulatory Commission amended its regulations in 10 CFR 35 concerning the medical use of by-product material to require medical licensees to establish and implement a quality management program (QMP). The overall goal of the QMP is to prevent errors in the medical use of by-product material.

This report is the result of an investigation by a team contracted by the NRC to review radiation therapy events. The purpose of this team is to obtain the necessary detailed information on selected events and perform an analysis of the causes, contributing factors, risk significance, and corrective actions.

The NRC obtains this information to help it evaluate the adequacy of the scope and depth of the QM rule.

Scope

The team investigation is limited to the administration of the prescribed radiation treatment. The team members review the facts of the event and compare them to the facility's normal process and the NRC's regulations.

The team members are tasked to describe the events, compare them to the requirements, analyze for the cause of the event and contributing factors, assess the risk significance, and describe and evaluate the licensee response.

The amount, type, and modality of radiation originally prescribed is a medical matter and, as such, is outside the scope of this investigation.

The precise financial obligations and relationships between the principals are a contractual and legal matter and, as such, is outside the scope of this investigation.

Event Overview

A 73-year-old white male was scheduled to receive a transperineal prostate ¹²⁵I implant. Although the Urologist and Radiation Oncologist involved thought they implanted 0.44 mCi seeds, they actually implanted 4.49 mCi seeds. One hundred and twelve seeds were implanted with a total activity of 502.88 mCi. The implant procedure went smoothly and good positioning of the seeds was documented. The activity problem was noted by the dosimetrist shortly after the procedure. The initial planned peripheral tumor dose (PTD) was 160 Gy. By inference of the factor-of-ten error in seed strength, the PTD achieved if the seeds were left in place would have been 1600 Gy over 1 year.

Detailed Description

Principals

| | |
|--------|--|
| Fac-1 | Facility-1 is the licensee. Fac-1 is a medium-sized community hospital. It has been licensed for brachytherapy for three months. This was the eighth procedure performed. |
| Uro-1 | Urologist-1 is affiliated with Fac-1. Uro-1 performed the implant and the mitigating radical prostatectomy. |
| Sur-1 | Surgeon-1 is a general surgeon affiliated with Fac-1. Sur-1 performed the mitigating, protective colostomy. |
| RSO-1 | RSO-1 is Fac-1's Radiation Safety Officer. RSO-1 is a diagnostic radiologist. |
| NMT-1C | NMT-1C is the Chief Nuclear Medicine Technologist at Fac-1. NMT-1C ordered the seeds from the supplier. |
| NMT-12 | NMT-12 is the second Nuclear Medicine Technologist at Fac-1 discussed in this report. NMT-12 received the seed shipment at Fac-1. |
| Fac-2 | Facility-2 is a large teaching institution. Facility-2 was under contract to Fac-1 to provide services of radiation oncologists, medical physicists, and dosimetrists for ¹²⁵ I transperineal, prostate brachytherapy. |
| Onc-21 | Radiation Oncologist-21 is affiliated with Fac-2 and is an authorized user at both Fac-1 and Fac-2. Onc-21 was present for the implant. |
| Onc-22 | Radiation Oncologist-22 is affiliated with Fac-2 and is an authorized used at both Fac-1 and Fac-2. Onc-22 consulted with Fac-1 personnel when they were planning mitigating action. |
| Dos-2 | Dosimetrist-2 is affiliated with Fac-2 and performed supportive services for brachytherapy services at Fac-1. Dos-2 loaded the sources that were of a different strength than specified in the written directive into the application needles. |
| RSO-2 | RSO-2 is Fac-2's Radiation Safety Officer. RSO-2 went to Fac-1 to assist during the mitigating prostatectomy and colostomy. |
| Sup-1 | Sup-1 is an employee at the source supplier's office. Sup-1 took the seed order from NMT-1C. |

Planning

The treatment plan was performed normally by Dos-2 at Fac-2 based on directions from Onc-21. Onc-21 signed the written directive on the 16th of the month. The written directive called for 112 seeds of 0.43—0.46 mCi ^{125}I per seed, but did not show the total activity. Dos-2 sent the written directive to NMT-1C by FAX at about 11:00 AM on the 16th.

Seed Acquisition

NMT-1C called the supplier by telephone at about noon on the 16th to order the seeds. A miscommunication between NMT-1C and the Sup-1 resulted in the order being entered as 4.3 – 4.6 mCi ^{125}I in the supplier's computer system. NMT-1C told the other nuclear medicine technologists that a package should arrive the next day. NMT-1C did not tell them the intended strength of the ordered seeds.

This was the eighth prostate brachytherapy at Fac-1. NMT-1C had made all previous orders from the same supplier without incident, but this was the first time that NMT-1C had spoken to Sup-1 in particular. Sup-1 wrote *04.3 – 04.6 mCi* by hand on the note sheet; however, *0.43 – 0.46* was entered in the computer. Sup-1 then deleted the original order from the computer and placed an order for 4.3 – 4.6 mCi seeds. The supplier's system required a backup confirmation for this order because of its size — approximately 500 mCi. Sup-1 called NMT-1C to confirm the order. Again, a miscommunication occurred and Sup-1 maintained the order was for 4.3 – 4.6 mCi seeds.

The 4.3 – 4.6 mCi seeds were shipped in accordance with the information in the supplier's computer. The package was received at Fac-1 on the 17th by NMT-12. NMT-12 performed appropriate surveys, opened the package, checked the label on the vial against the packing slip, and logged the vial into the storage area. The packing slip listed the seeds by the four lot numbers and gave the number, statistical activity information, and total activity of each group of seeds that were in the vial. The midpoint apparent activity for all lots was 4.490 mCi per seed calibrated for the 20th. It did not show the total number of seeds or total activity for the shipment. NMT-12 did not check the package against the written directive.

The supplier called Fac-1 later on the 17th to confirm that the package arrived and all was in order. This had not been done for the previous seven shipments, but was normal for the supplier for orders of this total activity.

Loading

On the 21st, Dos-2 went to Fac-1 to prepare for the implant. Dos-2 remove the 4.3—4.6 mCi seeds from storage and logged them out. The log sheet described the contents of the vial as 112 seeds of 4.49 mCi each for a total of 502.88 mCi. Dos-2 logged out the vial as 112 seeds of 502.88 mCi. Dos-2 took the vial to the operating room, sterilized the vial and contents, and loaded the needles with the 4.3—4.6 mCi seeds. The loading summary, on the loading plan, listed 110 seeds of 0.444 mCi. The implant summary, also on the loading plan, listed 112 seeds with a total activity of 49.73 mCi.

Implant

The transperineal implant was performed from 10:00 AM to 10:45 AM by Uro-1 and Onc-21. Dos-2 was present. Films taken after the implant showed that there was good seed placement throughout the prostate. Dos-2 performed the post implant survey of the patient at 10:45 AM and recorded the dose rate at 1 meter as 4 mR/hr.

Discovery

After the surgery, Dos-2 returned to the storage room to complete the log sheet and show the final disposition of the seeds. Dos-2 began to enter the total activity but stopped and recognized that the total activity was an order of magnitude higher than prescribed. Initially Dos-2 treated this as an error and began to line out the activity entries of 502.88 mCi and 4.49 mCi throughout the log sheet and replace them with 50.288 mCi and 0.449 mCi entries. Before finishing this, Dos-2 stopped and checked the vial and found that the seeds were listed as 502.88 mCi from the supplier. Dos-2 confirmed the actual seed strength with the supplier, then notified Uro-1 and RSO-1 of the error. The patient and the patient's family were notified shortly thereafter.

Mitigation

Initial dosimetry

The initial dose rate of the implant was 18.5 Gy/day to the intended implant volume.

First Surgery

Onc-21 was already traveling to Fac-2 when the discovery was made, so Uro-1 and RSO-1 consulted with Onc-22 at Fac-2 by telephone on the options open to them. It was decided to perform a radical prostatectomy. RSO-2 traveled to Fac-1 to advise during the operation. The operation was started about 1:30 PM. Uro-1 performed the retropubic radical prostatectomy with the assistance of Sur-1. Additionally, a C-arm¹ was used to see if there were any seeds remaining. There appeared to be a number of residual seeds in the pelvis; therefore, Uro-1 and Sur-1 removed any perirectal tissue that could be taken with careful dissection. Of the 112 seeds implanted, 69 were removed. One seed was transected in the operative field, and subsequent activity was detectable in the patient's thyroid. Potassium iodide was later given in an attempt to suppress further thyroid uptake of circulating ¹²⁵I. As intraoperative x-rays revealed, a significant number of seeds remained in the region of the urogenital diaphragm and rectum, and an appropriate decision to perform a protective colostomy was made. The colostomy was done by Sur-1. The procedure was finished about 3:00 PM.

Uro-1 and Sur-1 wore film badges but no finger rings during the procedure.

Interim Dosimetry (Following first surgery)

The patient was transferred to Fac-2 where more formal dosimetry on the remaining 43 seeds could be performed. Of the remaining 43 seeds, 27 were in the prostatic bed, 8 in the right upper perirectal area, 5 in the left upper perirectal area and 3 were in the left sacrum.

The maximum significant dose rate² by the mass of seeds low in the pelvis was about 0.5 to 0.6 Gy/hr (~13 Gy/day), and not much changed from the original dose rate, but this dose rate now encompassed a volume of only 23 cm³ (2.8 cm average dimension, approximately). The upper mass of seeds had a maximum significant dose rate of about 0.3 Gy/hr (7.2 Gy/day) on the patient's right side, and about 0.1

1 The C-Arm is a portable fluoroscope unit.

2 The Maximum Significant Dose, for dose rate calculations, is defined as the value of the highest isodose line that encompasses two or more seeds. These calculations are presented to compare the intensities of the radiation field at different times, but the results should not be interpreted as clinically significant, nor should they be used to compare this event to other cases since the MSD is strongly affected by the strength of the seeds. The medical effects to the patient will be treated in the next section.

Gy/hr (2.4 Gy/day) on the left. The right side enclosed a volume of approximately 7 cm³, and on the left about 1 cm³. The doses and volumes contain a larger uncertainty than usual for brachytherapy calculations (normally about 2%) because the films used were not taken under controlled conditions and lack the normal alignment information.

Through full decay of the seeds, the maximum significant dose delivered in the lower seed mass would have been about 1100 Gy; in the upper group about 1000 Gy; and, for the few seeds by themselves, about 200 Gy.

The maximum significant dose may not be a meaningful indicator of clinical effects. A normal prostate implant also gives very high doses. Looking at the "peripheral dose," where this implant intended to deliver 160 Gy at the periphery of a 5 cm diameter volume, for the same size volume this geometry would have given about 550 Gy to the lower seed mass. The upper mass is more diffuse, and a value of 160 Gy (i.e., normal for a prostate implant) may be a reasonable estimate at 5 cm diameter.

Second Surgery

The concentration of seeds remaining in the urogenital diaphragm area still represented the most serious area of concern for life-threatening complication; therefore, perineal exploration was undertaken, by Onc 21, 6 days following the initial implant. Fifteen additional seeds were recovered in this fashion, leaving a total of 28 in place with a total activity of 125.7 mCi. Of these, 12 seeds were in the perineum, 5 in the left upper perirectal area, 8 in the right upper perirectal area, and 3 in the left sacrum. (No change to the upper seeds.)

Final Dosimetry (Following all mitigating surgery)

The doses to the upper seed mass and the upper perirectal areas remained the same. The lower mass maximum significant dose was reduced to 400 Gy from 1100 Gy. The dose at the surface of a 5 cm diameter circle (size of original target) was reduced to 250 Gy from 550 Gy. The 250 Gy surfaces in the third dimension are only 2.3 cm apart top to bottom. The total dose delivered to the rectum and bladder ranged from 50-100 Gy, with a very small portion of the right rectal wall receiving up to 200 Gy and the base of the bladder about 150 Gy.

Table 1: Summary of Dosimetry

| Phase | Planned | Post Initial Implant | Post First Mitigating Surgery | Post Second Mitigating Surgery |
|---|---------|----------------------|-------------------------------|--------------------------------|
| Number of Seeds | 112 | 112 | 43 | 28 |
| Total Activity | 50 mCi | 502.88 mCi | ≈193 mCi | ≈126 mCi |
| Dose to decay for 5 cm diameter target volume | 160 Gy | 1,600 Gy | 550 Gy | 250 Gy |
| Dose to decay for maximum significant dose (lower seed bed) | | | 1,100 Gy | 400 Gy |

Medical Consequences

Unmitigated Patient Effect

The quantity of irradiation implanted was life-threatening to the patient. Undetected and without mitigative actions, the doses to the rectal, perineal, prostatic, and bladder tissues would have far exceeded tolerance. Without any recorded similar cases for comparison, but with doses exceeding standard tissue tolerance limits for a least a few centimeters from the implanted gland, general radiobiologic and physiological inferences can be made:

Prostate: Expected effects over the first several weeks might include progressive, intense dysuria, and urethral edema with subsequent difficulty initiating a urinary stream. Later effects might include hematuria and liquefactive necrosis of the gland, surrounded by areas of dense fibrosis in the periprostatic tissues and urogenital diaphragm. Loss of urinary sphincter control and impotence could be anticipated. Total urinary obstruction or fistula formation to surrounding viscera (rectum) would be likely. Pain from nerve entrapment or secondary severe genital edema might occur.

Bladder: The bladder would suffer early on from radiation mucositis causing dysuria, frequency, and hematuria. Disruption of the mucosal lining might later precipitate life-threatening hemorrhage. Outlet obstruction of the bladder neck would later lead to secondary hydronephrosis, renal failure, and death, barring medical intervention.

Rectum: Initial rectal urgency and perianal irritation would develop within several weeks, and might well progress rapidly to frank rectal wall ulceration, hemorrhage, sepsis, and death. If patient were to survive long enough, impairment of anal sphincter tone would be likely secondary to fibrosis and potential nerve damage.

Sacral Plexus Nerves: It appears that 3 seeds have migrated into the neural foramina of the sacrum, at separate sites around the left S2-3 nerve roots, perhaps via Batson's venous plexus. These nerve roots innervate the posterior femoral cutaneous nerve and, based upon point dose calculations of greater than 100 Gy at 1 cm from a point-dose seed, these nerve roots may be functionally impaired over the next 6-12 months. This impairment might cause permanent dysesthesias in the left leg.

Mitigated Patient Effect

Because of the mitigating effects of early discovery of the error and prompt removal of the bulk of the seeds, radiation effects to the rectum and bladder might include rectal edema, possible proctitis for several weeks, a late risk of rectal stenosis or rectal bleeding, painful cystitis, urethral stenosis, intermittent urethral or bladder ulceration or bleeding. The scattered locations of the remaining seeds will help reduce the overall tissue toxicity and dose. As noted previously, the left S2-3 sacral nerves will receive a dose likely to cause permanent impairment of function.

Although the additional surgeries were clearly indicated to save the patient's life, complications related to these surgeries might include those noted in Appendix A related to radical prostatectomy, as well as poor wound healing, poor urethral and anal sphincter tone/control, pelvic adhesions, and pelvic floor scarring/fibrosis. In addition, there is a risk of ensuing hypothyroidism over the next 2 years.

Staff Effects

Readings from collar badges worn by the medical staff during the surgeries are pending. Finger rings were not worn by the Uro-1 or Onc-21. Nevertheless, with the low energy of the ¹²⁵I seeds and the fact that they were inside steel trocars when in the operating room, as well as the limited time of the implant procedure, it is doubtful that these personnel exceeded their allowable doses during the initial implant

procedure. Another way to think of this is that they did "10-12 procedures," which is not an uncommon number for experienced implanters.

Of more concern is the additional dose the Uro-1 and Sur-1 were subjected to during the subsequent retropubic prostatectomy, in which considerable time was spent dissecting the tissues within the pelvis. Uro-1 tried to limit his hand dose by the use of invasive radiologist-style lead-lined gloves during the prostatectomy. It is doubtful there was any significant exposure to the other operating room or ward personnel, based upon the implant. Indeed, exposure calculations performed by RSO-2 for all other personnel involved at Fac-1 and Fac-2 indicate whole body and extremity doses were well within federal guidelines,³ with Dos-2 receiving the highest calculated dose of 278 mR whole body, and 2416 mR to the extremities. These doses are estimates, and have yet to be confirmed by badge dosimetry.

Using the Anderson nomogram, a 5.0 cm average diameter organ with 69 seeds would need seeds of 0.65 mCi each to deliver 160 Gy to the periphery of the prostate through decay. For a 160 Gy implant of ¹²⁵I (half-life 59.8 days), the first day will deliver:

$$160\text{Gy} \left(1 - e^{-\frac{(1\text{day})\ln(0.5)}{59.8\text{days}}} \right) = 1.84\text{Gy}$$

Thus, the peripheral dose rate in this case would be

$$\left(\frac{1.84\text{Gy}}{\text{day}} \right) \left(\frac{\text{seed}}{0.65\text{mCi}} \right) \left(\frac{4.4\text{mCi}}{\text{seed}} \right) = \frac{12.5\text{Gy}}{\text{day}}$$

Converting to rem/hr gives:

$$\left(\frac{12.5\text{Gy}}{\text{day}} \right) \left(\frac{\text{day}}{24\text{hrs}} \right) \left(\frac{100\text{rem}}{\text{Gy}} \right) = \frac{52\text{rem}}{\text{hr}}$$

From measurements, the gloves transmit a 0.195 portion of ¹²⁵I radiation. Assuming Uro-1 had the organ in his hand for 0.5 hour, the dose to his hand would be:

$$\left(\frac{52\text{rem}}{\text{hr}} \right) (0.195)(0.5\text{hr}) = 5.1\text{rem}$$

This is well within federal guidelines and should be clinically insignificant.

3 10 CFR 20 allows 5000 mR whole body and 50,000mR to the extremities per year

Corrective Actions

Immediate Corrective Actions

Shortly after the misadministration, Fac-1 administrators voluntarily halted the entire implant program pending detailed review.

Long-Term Corrective Actions

Long-term corrective actions have not yet been developed. A meeting of Fac-1 administration and RSO-1 is scheduled to discuss long-term solutions. Program agenda items include altering procedures for logging in sources with required comparison to the physicians written directive, as well as a need to "delineate more clearly" responsibilities of the various personnel from the two institutions involved with the implant, and discussion of whether or not to cancel the implant program permanently.

Comparison to Requirements

The NRC has specific requirements that apply to the medical use of by-product material. In this section those requirements are reviewed and the licensee's compliance with the requirements is evaluated. Only those requirements that are closely related to the primary cause and contributing factors for these misadministrations are discussed.

Quality Management Program

NRC Regulations

§ 35.32 Quality management program.

(a) Each applicant or licensee under this part, as applicable, shall establish and maintain a written quality management program to provide high confidence that byproduct material or radiation from byproduct material will be administered as directed by the authorized user. The quality management program must include written policies and procedures to meet the following specific objectives:

...(4) That, each administration is in accordance with the written directive; and

Evaluation

Although Fac-1 had a written QMP, the QMP did not provide written policies and procedures or assignment of responsibilities for brachytherapy.

Radiation Safety Officer

NRC Regulations

§ 35.21 Radiation Safety Officer

...(b) The Radiation Safety Officer shall:

...(2) Establish, collect in one binder or file, and implement written policy and procedures for:

...(v) Using byproduct material safely;

Evaluation

The only procedure found for receipt of brachytherapy sources was NMT-1C's handwritten note, posted on a hot-lab bulletin board above the work area, that described the steps to be followed when the seeds arrive.

Treatment Accuracy Verification

NRC Requirements

Quality Management Program

[See § 35.32(a)(3) above.]

NRC Guidelines

Regulatory Guide 8.33, C.3.2, All Other Brachytherapy Applications

3.2.3. The licensee should establish a procedure to verify, before administering the brachytherapy dose, that the specific details of the brachytherapy administration are in accordance with the written directive and plan of treatment. In particular, the radioisotope, number of sources, and source strengths should be confirmed to verify agreement with the written directive and plan of treatment.

3.2.5. The licensee should establish a procedure to have an authorized user or a qualified person under the supervision of an authorized user (e.g., a radiation therapy physicist, oncology physician, dosimetrist, or radiation therapy technologist) verify that the radioisotope, number of sources, source strengths, and, if applicable, loading sequence of the sources to be used are in agreement with the written directive and plan of treatment before implanting the radioactive sealed sources. The licensee may use any appropriate verification method, such as checking the serial number of the sealed sources behind an appropriate shield, using a radiation detector, using a dose calibrator, using color-coded sealed sources, or using clearly marked storage locations, i.e., one location for each source strength. The responsibilities and conditions of supervision are contained in 10 CFR 35.25.

Evaluation

There were no written procedures or checklists to ensure the sources' strengths were correct before implanting. There was an unwritten policy that the dosimetrist, in this case Dos-2, who prepares the treatment is to verify the source strength against the requirements of written directive, but not necessarily physically view the written directive. Dos-2 did, in fact, check the source strength, but did so incorrectly.

Notifications, reports, and records of misadministrations

NRC Regulations

§ 35.33 Notifications, reports, and records of misadministrations

(a) For a misadministration:

...(3) The licensee shall notify the referring physician and also notify the patient of the misadministration no later than 24 hours after its discovery, unless the referring physician personally informs the licensee either that he will inform the patient or that, based on medical judgment, telling the patient would be harmful. The licensee is not required to notify the patient without first consulting the referring physician. If the referring physician or patient cannot be reached within 24 hours, the licensee shall notify the patient as soon as possible thereafter. The licensee may not delay any appropriate medical care for the patient, including any necessary remedial care as a result of the misadministration, because of any delay in notification.

Evaluation

Prompt notifications were made to the referring physician and patient.

Event Analysis

Discussion of Observed Contributing Factors

A number of factors contributed to staff performance. This discussion will present contributing factors and observations concerning the medical misadministration. The possible contributing factors at the pharmaceutical supplier are not discussed because the supplier personnel were not interviewed and their work environment and processes were not examined by this team. A summary of events leading to the misadministration is given in Figure 1. This figure contains principle events and factors that contributed to those events. Each of the performance shaping factors are discussed in the following sections.

Procedures

Procedures, in this context, are step-by-step instructions for carrying out specific actions. Procedures are the designated process used to accomplish a task. Procedures are developed and designated to ensure correct performance and standardized performance. Procedures are not necessarily written down, although they usually are written in order to aid the performer or serve as a standard or reference. Several issues related to procedures were identified as contributing factors to the misadministration.

1. Some procedures were not standardized and stabilized.

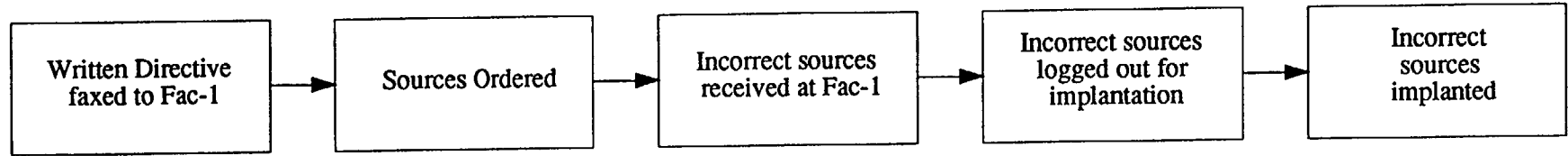
The prostate implant program at Fac-1 was relatively new; this was only the eighth implant. The procedures for accomplishing necessary tasks related to ordering, receiving, storage, and inventory of nuclear implant material were still evolving. For example, for the first three receipts of packages containing ^{125}I seeds, the nuclear medicine technicians at Fac-1 surveyed the unopened package, but did not open the package. Then the procedure evolved to include the nuclear medicine technologists opening the package. Similarly, the form for recording the inventory was changed after the sixth implant. Personnel reported that the original "brachytherapy log seed accountability" form was not serving their needs, and was therefore changed. Therefore, the actual activities being performed by the nuclear medicine technologists were changing in small ways every few times the implant surgery was performed. The procedures were not stable, were not yet routine, and did not have written instructions or checklists to support the technicians in the performance of their tasks.

The ordering of ^{125}I seeds followed a routine, but the specifics of the order were not necessarily the same each time. NMT-1C reported ordering by reading the numbers on the directive, but the numbers on the written directive were not necessarily standardized (e.g., the activity for each seed might or might not have a preceding zero in front of the decimal).

2. Issue of reporting any "problems".

As stated by NMT-1C, the procedure for any problems encountered was to report them to RSO-1. The issue is what constitutes a problem. NMT-1C reported that shortly after the initial order was placed, a second phone call from the supplier was received and a second order confirmation number was given to NMT-1C by the supplier's operator. (If the supplier's operator explained the verification call was made because of the unusually large activity of the order, the error might have been discovered before the seeds were shipped.) NMT-1C identified this as odd. The issue then becomes what degree of oddity constitutes a problem and must therefore be reported to RSO-1.

Events



Contributing Factors

- Radiation Oncologist and Dosimetrist located as Fac-2.
- Verbal order not followed by written confirmation (fax).
- Miscommunication with supplier.
- Distributor did not explain why order was verified.
- Procedure did not require NMT to check against written directive.
- NMT unfamiliar with appropriate source strengths.
- NMT not aware of details of order.
- Receiving procedures evolving.
- Lapse by Dosimetrist.
- No written checklist.
- No verification/second check.
- No means for authorized user to verify seed strength.

12

Performance Shaping Factors

Management

Communications
Procedures
Training

Procedures
Communicatons
Training
Management

Procedures
Ergonomics

Ergonomics

Figure 1. Summary of events leading to the misadministration.

3. Procedure to verify the source strength.

Neither Fac-1 nor Fac-2 has any written procedure or practice that calls for a verification or second check of the strength of the sources used. Unwritten practices did call for a check, and all of the principals independently described the procedure identically — that the dosimetrist checked the activity against that used in planning at the time of loading the needles. Even the person making the error thought that this was the procedure.

Communications

Several factors associated with communications within or among organizations were identified.

1. Verbal communication was not always followed by written communication.

The order for the ^{125}I seeds was made verbally by NMT-1C during a telephone call to the supplier. By the result, we know that a miscommunication occurred. If the spoken communication had been followed by a written, confirming facsimile of the verbal order, it is likely that the verbal miscommunication could have been identified and corrected.

2. Communication among the nuclear medicine technologists as to what the expected package contained.

After the NMT-1C placed an order for ^{125}I seeds by telephone, the other nuclear medicine technologists were informed that a package would be arriving. No information was given as to what was ordered and expected within the package. In this case, the person receiving the package was a different person than the person placing the order. The person receiving the package did not know what was expected in the package.

3. Communications among multiple organizations can be complex.

Communications among several organizations can result in assumptions being made as to who has what information. Information may be communicated between organizations, but then not fully disseminated within organizations. Individuals may not be fully cognizant of other organizations and therefore not aware of, or uncertain of, how specific tasks are accomplished at one location versus another location.

Key communications in this misadministration occurred among two hospitals and a supplier. Communications were made verbally (phone and in person) and in writing. Some original documents were generated in one location and used in another location. During the interviews, it was not always clear where the originals of some documents were located. Assumptions as to what tasks would be performed were made because communications were not sufficiently detailed. Some of these assumptions were incorrect and contributed to this event.

Training

Training of Fac-1 nuclear medicine technicians and nursing staff was developed and conducted, at least in part, by personnel from Fac-2. Of particular interest here is the training of the nuclear medicine technicians. The training outline included general discussion of radioisotopes and some required tasks such as surveying for radioactivity. Procedures, record keeping, and job aids were changed over time (as discussed above). Fac-2 personnel reported that the Fac-1 personnel had been trained, asked to do certain tasks to allow familiarization, and then given tasks of increased scope, in essence allowing the Fac-1 personnel to gain experience slowly. The NMT-1C reported that the nuclear medicine technologists believed this process resulted in them being uninformed and inadequately trained.

The issue is whether the training was intended to show individuals specific, concrete tasks and then practice those specific tasks, performing only those tasks, or if the training was intended to introduce the

context in which specific tasks are performed (i.e., the "larger picture"). One approach is not necessarily inherently better than the other; they have different uses and different outcomes. When taking one approach to training, it should be clearly understood what the consequences will be. If individuals are trained only to do specific, concrete tasks, then that is what they will do.

Ergonomics

Often, ergonomics is referred to as human factors engineering and deals with machines or pieces of equipment designed for use in the job. In this case, machines did not play an important part in this event. Of interest is the design of forms and job aids used, specifically, the form for the written directive and the inventory log. The three values of interest and importance are: 1) the number of seeds, 2) the activity (average or range) of each seed, and 3) the total activity of the seeds. The total activity of the seeds is calculated by multiplying the number of seeds by the average activity of each seed. All three numbers are important, and each provides a way to check the accuracy of the sources against the written directive.

1. Forms did not consistently require similar information.

The written directive lists the number of seeds and activity of each seed. The main portion of the inventory log lists the number of seeds and total activity of the seeds. (The average activity per seed is recorded on the top portion of the form, but is not given on each individual line of the log.) The label on the vial in which the seeds were delivered lists the number of seeds, the range of individual seed activity, and the total activity of the seeds. Not all the forms used required all these pieces of information on the seeds.

2. Sources are not visually distinguishable.

The ¹²⁵I seeds themselves are outwardly identical regardless of their activity. There is no visual indication that the activities of some of the seeds are an order of magnitude higher than others.

Management

An organizational factor contributing to the event was the contractual arrangement among the organizations and the clarity of who was responsible for aspects of the implant program. Fac-1 was the licensee, but there was a belief and understanding that the contracted Fac-2 was providing the program. Fac-2 believed that they were contracted to provide a service to Fac-1, but it was Fac-1's program. In some aspects, it appears that assumptions were made as to what would be carried out and by whom. For example, at Fac-2 the health physics technicians verify the strength of the sources on receipt, but do so in accordance with unwritten policy. It was assumed by RSO-2 that the nuclear medicine technologists at Fac-1 were verifying the labeled strength against the written directive, but not counting the seeds. The nuclear medicine technologists at Fac-1 reasoned that they were only to do what they had been directed to do and they had not been told to verify the sources against the order.

The coordination of responsibilities and activities needs to be clearly delineated and communicated (as mentioned previously).

Conclusions

Medical

Mitigative actions by numerous professionals involved have dramatically decreased the patient's risk of mortality, assuming he develops no perioperative complications. Some morbidity, however, is likely due to the extensive intervention required. Careful follow-up and attention to the rectum, bladder, perineum, anal and urinary sphincters, sacral nerves, and thyroid gland are imperative, as dysfunction of any of these structures may occur over the next few months to years, and may require further medical or surgical intervention.

From the initial dosimetry calculations, mitigative surgery probably could have been delayed a day or two if additional planning and preparation would have allowed the removal of more tissue around the prostate at the initial surgery.

Risk Analysis

Proximate Cause

The proximate cause of this misadministration was the lapse⁴ made when Dos-2 did not correctly verify the seeds were of the proper strength at the time of logging the seeds out of storage at Fac-1.

Barriers

Each of the factors in the previous section can be seen to have contributed to the misadministration. A clear way of looking at the event as a whole is to identify the ultimate points of failure and what barriers were in place (or not in place) to prevent a single point failure from causing a misadministration. A barrier can be a physical, engineered barrier, but can also be an administrative barrier. Three primary failures to protect against are: 1) giving the wrong dose, 2) giving dose to the wrong patient, and 3) giving the dose at the wrong anatomical site. In this case, the failure occurred in giving the wrong dose.

Reviewing the event suggests several places in the entire process where a barrier could have been placed to prevent the error that occurred. Clearly, if there had not been a miscommunication during the ordering process, then the correct activity seeds would have been received. An administrative barrier here would be to confirm the verbal telephone order with a written communication (i.e., a facsimile of the order). This could be done by either (or both) the hospital placing the order or the supplier receiving the order. To remove another potential for transcription error, the written directive itself could be sent to the supplier by facsimile.

Given that the wrong activity seeds were sent, a second barrier could be an inspection when the package was received. If all nuclear medicine technologists at Fac-1 were aware of what to expect in the package, and if they compared the received package with the original written directive, there would be another administrative barrier. If the dosimetrist compared the original written directive to the inventory log, there would be a third barrier. An independent check of the inventory being removed from storage to the operating room would be another barrier. (Although it should be noted that this independent check was not a normal routine procedure at Fac-2.) Logging the number of seeds, the activity of each seed and the total activity on each inventory line may have provided another check.

4 Slips and lapses are errors which result from some failure in the execution of an action, regardless of whether or not the plan that guided them was sufficient to attain the objective.

Independent checks and verifications are not duplication of effort, but can be administrative barriers, that is, objects that provide an opportunity to prevent an error. Independent checks and verifications may mean checks performed by different people or performed at a different time and place (or both different people and a different time and place). In quantitative risk analysis, credit is given and human reliability is increased by independent checks.

Whenever possible, barriers should be part of a written policy, even if the policy is a checklist. (The written checklist is a memory aid for the performer, it provides another barrier — the performer asking "Did I actually perform this step?"). All barriers would have to fail in order to administer the wrong dose. Certainly, this is not impossible, but it is less likely with well-placed and administered barriers.

Lessons Learned

Processes that have a high consequence should be reviewed. Points in the process where a single failure can lead to the consequence should be provided with barriers to prevent the propagation of the error through the process.

Recommendations

Fac-1 has an active Radiation Safety Committee, of which a Fac-2 Radiation Oncologist is a member. Committee attendance records, however, fail to show any attendance by the Radiation Oncologist, or direct input from him. If the brachytherapy program is to continue at Fac-1, more direct interaction of the Radiation Oncology staff from Fac-2 in committee proceedings is imperative.

Fac-1 had no formal Quality Management Program for brachytherapy services. The results of the NRC sponsored review of the Fac-1 QMP, which arrived days after the misadministration,⁵ should be reviewed before resumption of implant services.

Dose estimates to the operator involved would have been much more accurate and useful had finger rings been used. This needs to be emphasized as part of the QM Program.

Lack of ability to easily discern standard strength ¹²⁵I seeds from high-activity seeds,⁶ which were inadvertently used in this case. Any seed less than 1.0 mCi should be identifiable by color or other visually detectable means as different from the high-activity seeds. This will require manufacturer input and assistance, but would go a long way in helping prevent accidental use of these special seeds.

5 The results of the NRC sponsored review of the Fac-1 QMP arrived several days after the misadministration. It said, in part:

Fac-1's procedures did not require brachytherapy written directive ... including source strengths.

Procedures did not ensure that each administration is in accordance with the written directive.

Procedures should include a requirements for verification, before administering each brachytherapy dose, that the specific details of the administration are in accordance with the written directive and plan of treatment. The ...source strengths ... should be confirmed by the person administering the brachytherapy treatment to verify agreement with the written directive and treatment plan.

6 These "high activity" seeds only came into being in the early 1980s in response to a need for a removable source with good radiation protection properties—these seeds are used almost entirely for temporary implants, especially in areas like the brain and breast.

Appendix A Prostate Cancer Background

Prostate cancer is a common malignancy, with 165,000 new cases diagnosed and 35,000 deaths estimated in 1993 in the United States.¹ Most newly diagnosed cases have tumor confined to the region of the prostate gland. Although selected patients may be simply observed following diagnosis, most patients with such locally-confined cancers are offered aggressive curative treatment such as radical prostatectomy, external-beam radiation therapy or radioactive implant (permanent: ¹²⁵I or ¹⁰³Pd, or temporary ¹⁹²Ir).

Treatment options are discussed with the patient in detail, including the risks and benefits of each procedure. For example, radical prostatectomy entails a 72% risk of subsequent impotence and a 42% risk of at least occasional urinary incontinence,² with a 0-2% risk of perioperative mortality.³ External-beam radiation treatments carry a 3% risk of chronic intestinal complications (diarrhea, proctitis, anal stricture, rectal bleeding), and 7% risk of urinary complications (hematuria, cystitis, urethral stricture), and a very low risk of procedure-related mortality (0.2%).⁴ ¹²⁵I seed implantation performed from a suprapubic laparotomy approach entails a 1-8% risk of perioperative complications (bleeding, infection), an 8% risk of chronic bowel complications (bleeding, proctitis), a 6% risk of bladder complications (hematuria, dysuria, urgency, or incontinence), and a 10% risk of impotence.⁵ There has been a recent trend to avoid invasive surgery by implanting the seeds directly into the gland and surrounding tissues using a transperineal template to direct needles into the prostate under transrectal ultrasound guidance. This approach has allowed source placement with accuracy at least as good as the open laparotomy approach, and can be done as an outpatient "day-stay" procedure with regional anesthesia. The latter approach was used in this misadministration event.

Bibliography

1. Boring, CC, Squires, TS, Tong, T., "Cancer Statistics, 1993," CA 43, 7-15, 1993
2. Murphy, GP, Mettlin, G, Menck, H, Winchester, DP, "National Patterns of Prostate Cancer Treatment by Radical Prostatectomy: Results of a Survey by the American College of Surgeons Commission of Cancer," submitted to J Urol, 1994
3. Hanks, GE, "External-beam Radiation Treatment for Prostate Cancer: Still the Gold Standard," Oncology, March;79-90, 1992
4. Lawton, CA, et al, "Long-term Treatment Sequelae following External-Beam Irradiation for Adenocarcinoma of the Prostate: Analysis of RTOG Studies 7506 and 7706," Int J Radiat Oncol Biol Phys; 21, 935-939, 1991
5. DeBlasio, DS, et al, "Permanent Interstitial Implantation of Prostatic Cancer in the 1980s," Endocurietherapy/Hyperthermia Oncol 4, 193-201, 1988.

Appendix B

Typical ¹²⁵I Transperineal Implant Procedure

Preplan

After suitable candidate has consented to the implant procedure, he is placed in the proper implant position, and a transrectal ultrasound apparatus is positioned in the patient's rectum. Detailed outlines of the location of the gland including contours at several gland levels are obtained. Next, computerized treatment planning using these contours to reconstruct the gland dimensions allows the dosimetrist to calculate the proper seed quantity, strength, and spacing to achieve the target dose specified by the authorized user (Radiation Oncologist).

Seed Acquisition

After plan is reviewed/approved by the Radiation Oncologist, the dosimetrist or physics staff arranges for ordering the seed quantity and strength based upon a physician's written directive. In general, seeds are ordered in a strength of 0.4-0.6 mCi/seed in sufficient quantity to deliver a total dose of 160 Gy to the periphery of the gland over 1 year. Once the seeds are shipped to the facility, the physics or dosimetry staff log in the sources to the facility. Implicit in this procedure is not only making sure the number of seeds received actually matches the number on the shipping label, but also matches the requested number and strength ordered, as given on the written directive.

Preparation for Implant

Based upon the preplanned dosimetry, sterilized seeds and spacers are positioned in implant needles or in cartridges that are later attached to the implant needles. These loaded needles or cartridges are then transported to the operating room for the implant itself. Seeds are logged out of the "hot lab".

Implant

Patient is anesthetized and placed in the implant position (known as the lithotomy position) identical to that used for preplanning. The transrectal ultrasound equipment is properly positioned along with the transperineal guide template. The grid coordinates of the template are matched to the preplan, and the urologist then places implant needles into the perineum percutaneously to a proper depth determined by ultrasound guidance. A steel trocar is used to leave the seeds behind, in the tissues, as the needles are withdrawn. After the procedure the only external evidence of the procedure is the small puncture sites of the needles, which heal rapidly. Personnel involved in the procedure should wear appropriate body and ring badges to allow for accurate measurement of exposure.

Post-Procedure

Unused seeds are returned to the "hot lab" and logged back in, stored for decay, etc. Needles, dressings, and the operating room are cleared by Geiger counter, and these surveys are documented. Days to weeks following the implant, the patient is brought back for final dosimetry based upon the actual positioning of the implanted seeds seen on orthogonal radiographs. Badges are read and reviewed by medical physics (exposure is usually minimal to staff and operators due to the weak nature of ¹²⁵I, 27Kev, the shielding provided by the needles and cartridges, and the shielding afforded by the patient's own tissues. The patient is instructed to screen his urine for any excreted seeds, along with appropriate handling and notification procedures in that event.