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4 July 1994

Dr. Ronald Bellamy
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475 Allendale Road
King of Prussia, PA 19406

Dear Ron:

Attached is a copy of my medical impact assessment of the recent Backus Hospital misadministration event.

The original is being forwarded to Jim Tortorelli at EG&G Idaho via Federal Express on 5 July 1994 for use in his report, but Sattar indicated that you'd like to get a preliminary look at the medical part of the document. I thought it might be helpful in preparing the final report to provide some background about this disease, relative risks of other treatment approaches, etc., and these are incorporated into the report as well.

I still have not received independent dosimetry assessment from Bruce Thomadsen in Wisconsin, but was able to get the latest Yale dosimetry on 1 July FAX'd to me. It is upon this information that I have based my assessment, and in the interest of time have decided to forward my report now. If any radical changes come to light following Bruce's analysis, I will amend the document accordingly.

Hope this is helpful to you. Please let me know if you have any further questions. I'll be at (707) 423-7691 for the next two weeks if you need to reach me.

Sincerely,

Douglas W. Johnson, M.D., F.A.C.R.

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**MEDICAL IMPLICATIONS REPORT IN SUPPORT OF EG&G/NRC MISADMINISTRATION INVESTIGATION--BACKUS HOSPITAL NORWALK, CT**

4 July 1994

## I. BACKGROUND

Prostate cancer is a common malignancy, with 165,000 new cases diagnosed and 35,000 deaths estimated in 1993 in the Unites 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: I-125 or Pd-103, or temporary: Ir-192).

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 a 7% risk of urinary complications (hematuria, cystitis, urethral stricture), and a very low risk of procedure-related mortality (0.2%).(4) I-125 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.

## II. TYPICAL I-125 TRANSPERINEAL IMPLANT PROCEDURE

A. 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).

B. SEED ACQUISITION: After plan is reviewed/approved by the Radiation Oncologist, the dosimetrist or physics staff arrange 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 16,000cGy 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.

C. PREPARATION FOR IMPLANT: Based upon the preplanned dosimetry, sterilized seeds and spacers are positioned in implant needles or in cartridges which 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".

D. 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.

E. 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 I-125, 27Kev, the shielding provided by the needles and cartridges, and the shielding afforded by the patient's own tissues. Patient is instructed to screen his urine for the rare seed which is excreted, along with appropriate handling and notification procedures in that event.

III. **RECORDS REVIEWED:** Backus Hospital inpatient hospital chart, implant preplan, post-implant and post-mitigative surgery dosimetry, Backus Hospital contracts with consulting Yale/New Haven Medical Center, Backus Hospital Radiation Safety Committee minutes, Backus inservice program agenda and various attendant training forms, notes from preliminary NRC investigation team.

IV. **STATEMENT OF MEDICAL PROBLEM:** 73 year old white male was scheduled to receive a transperineal prostate I-125 implant. Although the Urologist and Radiation Oncologist involved thought they were implanting 0.449mCi/seed, they in actuality were implanting 4.49mCi/seed. A total of 112 seeds were implanted with a total activity of 502.88mCi. The implant procedure went smoothly and good positioning of the seeds was documented. The activity problem was noted by the dosimetrist following the procedure. The initial planned peripheral tumor dose (PTD) was 16,000cGy. By inference of the factor of ten error in seed strength, the PTD achieved if the seeds were left in place was 160,000cGy over 1 year.

Although details of the sequence of events leading to this event are outlined by other team members, the critical deficit lay in the failure of anyone (nuclear medicine staff, dosimetrist, physicist, physician) to ever compare the strength of seeds received to the strength of seeds ordered by the Radiation Oncologist.

V. **UNMITIGATED POTENTIAL MEDICAL IMPACT (PATIENT):**

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. I am unaware of any recorded similar cases to compare with, but with doses exceeding standard tissue tolerance limits for at least a few centimeters from the implanted gland, general radiobiologic and physiological inferences can be made:

A. 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.

B. 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.

C. 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.

D. 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 10,000cGy at 1cm 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.

**VI. MITIGATING ACTIONS:** To the credit of the Urologist, dosimetrist, and Yale personnel, action was undertaken shortly after the error was discovered. Within 4 hours, the patient was back in surgery--this time for a radical prostatectomy in an attempt to remove the majority of the seeds. Sixty-nine seeds were recovered in this fashion. One seed was transected in the operative field, and subsequent activity was detectable in the thyroid. SSKI was later given in an attempt to suppress further thyroid uptake of circulating I-125. 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 patient was transferred to Yale/New Haven where more formal dosimetry on the remaining 43 seeds could be performed. The concentration of seeds remaining in the urogenital diaphragm area still represented the most serious area of concern for life-threatening complication, and a perineal exploration was undertaken 6 days following the initial implant. Fifteen additional seeds were recovered in this fashion, leaving a total of 28 in place (125.7mCi): 12 in the perineum, 5 in the left upper perirectal area, 8 in the right upper perirectal area, and 3 in the left sacrum. Other remedies were considered, including insertion of a "radioprotective agent" on a tampon into the rectum, but this was felt to be impractical due to the chronic low dose rate of the I-125, uncertain uptake of the agent into the rectal wall, and lack of convincing evidence that it would work.

**VII. MITIGATED EXPECTED MEDICAL IMPACT (PATIENT):** Because of the mitigating effects of early discovery of the error and prompt removal of the bulk of the seeds, updated Yale dosimetry predicts the total dose delivered to the rectum and bladder to range from 5000-10,000cGy, with a very small portion of the right rectal wall receiving up to 20,000cGy. Radiation effects to those structures 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 the initial background section 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. I have discussed the concerns regarding sacral nerve injury with Dr. Ken Roberts on 1 July 1994, and suggested that he get neurosurgical opinion regarding impact of loss of nerve function, as well as feasibility or reasonability of attempted neurosurgical resection/removal of the seeds. Further surgeries to attempt additional seed resection from the pelvic soft tissues might entail more risk to the patient than benefit, at this point.

**VIII. EXPECTED MEDICAL IMPACT (STAFF/OPERATORS):** Readings from collar badges are pending. Finger rings were not worn by the Urologist or Radiation Oncologist. Nevertheless, with the low energy of the I-125 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 urologist was subjected to during the subsequent retropubic prostatectomy, in which considerable time was spent dissecting the tissues within the pelvis. The urologist 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 survey measurements of 4mr/hr at 1 meter from the patient measured shortly after the implant. Indeed, exposure calculations performed at Yale (Dr. Michael Bohan) for all personnel involved at Yale and at Backus Hospitals indicate whole body and extremity doses were well within Federal Guidelines, with the dosimetrist receiving the highest calculated dose of 278mR whole body, and 2416mR to the extremities (5000 mR whole body and 50,000mR extremity allowed per year). These doses are estimates, and have yet to be confirmed by badge dosimetry.

**IX. BACKUS HOSPITAL PLANS TO PREVENT REPEAT OF MISADMINISTRATION:** Shortly after the misadministration, Backus Hospital administrators decided to halt the entire implant program, pending detailed review. A meeting of administration and the Radiation Safety Officer is scheduled on day 10 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 on whether or not to cancel the implant program permanently.

**X. UNIQUE CIRCUMSTANCES/RECOMMENDATIONS:** Several items contributed to the misadministration:

A. The I-125 implant program was new to Backus Hospital, and this was only the eighth case performed. Personnel were not yet proficient enough with the whole process to realize who was responsible for what (specifically between the Backus Nuclear Medicine department and Yale dosimetry), and to recognize an "abnormal" quantity of isotope for the indicated procedure. Nuclear Medicine personnel admitted that they did not feel adequately trained in their understanding of the proper use of the material.

B. Procedures for ordering and receiving the I-125 were inadequate, and in fact were in a state of flux prior to this implant. Procedures for comparing the received material activity to that ordered by the Radiation Oncologist did not exist.

C. Lack of communication precipitated lack of understanding and lack of procedures formalizing responsibilities between the Hospital and Yale/New Haven Medical Center.

D. There was confusion over the strength of seeds ordered over the telephone, as evidenced by the findings of the initial investigators. This might be obviated by the requirement for a FAX confirmation of the order (physician's

written directive) to the manufacturer, prior to shipment of seeds.
E. Backus Hospital has an active Radiation Safety Committee, of which a Yale Radiation Oncologist is a member. Committee attendance records, however, fail to show any attendance by a the Radiation Oncologist, or direct input from him. If the brachytherapy program is to continue at Backus, more direct interaction of the Radiation Oncology staff in Committee proceedings is imperative.
F. Although Backus Hospital staff were provided a comprehensive initial inservice, no records exist to document indoctrination of new staff subsequently, or recurrency training as an on-going policy. This should be addressed.
G. Backus Hospital had no formal Quality Management Program/Policies for brachytherapy services that I saw. If this is indeed the case, the situation should be corrected prior to resumption of implant services.
H. Our dose estimates to the operator involved would have been much more accurate and useful had he worn finger rings. This needs to be emphasized as part of the QM Program.
I. Lack of ability to easily discern "standard" strength I-125 seeds from "high-activity" seeds, which were inadvertently used in this case (of note, 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 were and are used almost entirely for temporary implants only, especially in areas like the brain and breast). I would recommend that any seed greater than 1.0mCi be identifiable by color as different from the standard seeds. This will require manufacturer input and assistance, but would go a long way in helping prevent accidental use of these special seeds.

**VIII. MEDICAL SUMMARY:**

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 is 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.

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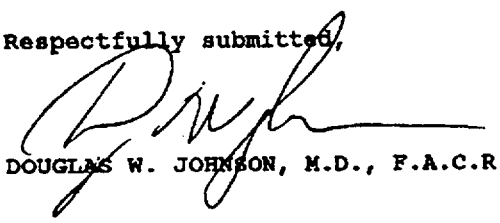
Respectfully submitted,



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