Medical Event Discovery: 2/8/18

Name of Prescribing Physician:

Lawrence Sheplan, MD

Brief Description of Event:

On 1/24/18 an apparent unexpected skin reaction is noticed by the Brachytherapy nurse before the third of three treatment fractions. An investigative process was initiated to determine the cause as well as additional safeguards put in place to attempt to minimize risks while a root cause could be identified (see below). On this date the skin reaction observed was a symmetric linear hyper-pigmentation on bilateral thighs with no evidence of dry or moist desquamation. At this point it was unclear if it was radiation related. The patient was placed on close observation. She was set up to be seen in follow-up by her referring physician who reportedly saw her on 1/30/18 and recommended treatment with steroid cream and aloe vera. Reportedly (per our conversation) with the referring physician, at that time there was still no evidence of dry or moist desquamation. She was scheduled to be seen in follow-up by her prescribing physician on 2/2/18 but she was unable to make it to the appointment and rescheduled it to 2/6/18. On 2/6/18 patient was seen by him in follow-up and skin reaction had progressed to moist desquamation (approximately 5cm long by 1.5 cm wide). He informed the patient of fact that we believe her skin reaction to be a radiation related side effect that was caused by a dose that was erroneously delivered to the area between her thighs (where instead it should have been delivered to the vaginal vault). She was also given an explanation similar to the one summarized below of our hypothesis of what occurred. She was told we would continue to see her every 2-3 days (or as needed) until her skin reaction heals. This was reported to the safety monitoring committee on the scheduled weekly meeting of 2/8/18. Following review of the aforementioned information, it was now clear that the reaction was radiation related, and the incident report was carried out on that same day as per protocol.

Why the event occurred:

By necessity the incident must have happened during one of the first 2 treatment fractions. Both administrations were retrospectively reviewed in depth and showed no deviations from protocol. There was no alarm or alert from the system. Cylinder was placed as per protocol. Pre-treatment film verified cylinder position. The physician reviewed pre-treatment films and then entered the room and verified the catheter position and the transfer tube connections to cylinder and afterloader as per protocol. Pre-treatment safety checks and plan review were carried out and treatments were delivered without incident. The treatment plan, dwell positions and time of radiation delivery were all normal as reported by the post-treatment documentation of the system. The nurse who disconnected catheters and removed the cylinder did not report any abnormality. The patient did not immediately report any

abnormalities, though now in retrospect when questioned, mentions she felt some irritation in the inner thigh area around the date of the second fraction.

The cylinder has multiple parts, cylinder base, locking nuts, “outer tube”, cylinder segments and the “internal catheter” that connects to the transfer tube.

Retrospectively we have determined the most plausible scenario is as follows. Sometime after the pre-treatment film which verified the cylinder position and “outer tube” placement and after the physician visually verifying the catheter position and transfer tube connections, but before or shortly after the start of the treatment, the “internal catheter” slid out of the cylinder applicator and ended up between the thighs of the patient. This is not a normal function of the equipment, as this catheter is supposed to be fixed in place via a type of pressure coupling once the cylinder is assembled, and the locking nut tightened. As the position was visually verified, we believe that the locking nut was likely too loose (of note, this nut CAN be overtightened to the point it will block transit of the source, so it cannot be “fully tightened” and must be done to an intermediate level of tightness which can be difficult to gauge) and either patient motion, or possibly the weight of the sheet (used for patient warmth) may have put weight on the transfer tube and this pulled on the “internal catheter” and caused it to slide out. At that point the patient’s thighs must have held it in place. The conclusion that it happened before, or early, during the treatment is supported by the length of the skin reaction which was noted to be approximately 5cm in length (similar to the active length in the treatment plan). We believe that the “internal catheter” must have been outside of the applicator (having fallen to the treatment table when the patient separated her thighs) when the nurse entered the room to retrieve the cylinder and disconnect the transfer tube, however, she does not recall having seen the “internal catheter” out of place. This is not something that the nursing staff had been told specifically to be on the lookout for. The dose estimate for skin directly in contact with the surface of the “internal catheter” is between 51.54 Gy and 85.55 Gy.

Effect on the individual who received the administration

Objectively: She was noted to have hyperpigmentation and irritation without evidence of desquamation for approximately 12 days (from 1/24/18 to 2/5/18). She the developed moist desquamation around 2/6/18 and continued to be monitored. The next visit was on 2/13/18 with Dr. Sheplan where she was noted to have started the process of re-epithelialization with a central area of about 1cm width of moist desquamation, a halo of about 1cm around this where the desquamated area showed signs of re-epithelialization, and a further ~1cm area of hyperpigmentation where no desquamation took place. She is still actively being monitored via phone encounters as on this visit she informed us of a trip to Florida for about 3 weeks that she had previously planned. She was asked to keep us in the loop as to her recovery and any new issues via phone during her time away. Dr. Sheplan informed her that this report was being drafted and would be available to her if she requested it. When queried she denied having noted or felt anything out of place before, during or after either of the first two fractions.

Subjectively: To date she has reported irritation and discomfort in the area between her thighs. She has not required narcotic pain medications and has managed it with skin creams and over-the-counter

NSAIDs. It has not impeded her ADLs, but she reports that it is very bothersome with prolonged walking as it coincides with the area where her thighs rub together.

Actions taken to prevent recurrence

Immediately when the possibility of an incident was noted, additional temporary safeguards were implemented until a clearer picture emerged.

Weekly safety monitoring committee meetings were instituted (on Thursdays). Best-case, worst-case and most-likely scenarios were developed for the dose the patient could have received. Given that the worst-case scenario (which would clearly be reported if confirmed) should without a doubt present moist desquamation, the committee decided that due to lack of other clear evidence as to what happened, the worst-case scenario (as hypothesized above) could be confirmed using the patient's own skin reaction as an "in-vivo" dosimeter. The patient was set-up to be seen every 2-3 days for close monitoring and case was discussed by the committee as new information became available.

Additional safety checks put in place during cylinder HDR applications included:

Pre-treatment films will now include a guide wire inside the applicator in order to make the "internal catheter" visible on the films.

Change in our standard protocol in order to mitigate the possibility of inappropriate assembly of the cylinder, and to minimize the time window between insertion and treatment where the catheter could "slip out": Instead of nursing staff assembling and inserting the applicator and then the physician inspecting it prior to administration (pre-existing protocol), now the physician personally assembles and inserts the applicator, connects to transfer tube and afterloader, and immediately proceeds to administration. This will be revised once the new applicator is available.

Nursing staff, physician staff and all brachytherapy-related personnel were re-trained as to an "if you see something, say something" culture of reporting mistakes in a non-punitive environment and reminded of the importance for patient safety of immediately notifying anything off-protocol or otherwise abnormal.

Purchase of new design applicator which no longer contains a removable "inner catheter" (the presumed point of failure is no longer part of the current generation applicator design).

Pre- and post-treatment checklist designed to include verification of: cylinder position, "internal catheter" position, transfer tube connection to "internal catheter", port film review of position of cylinder and presence of guide wire and transfer tube connection to afterloader.

A fully revised protocol for cylinder patients is being written-up to include the above and any other recommendations that result of the investigation and reporting of the incident.