Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Use of Isotopes (ACMUI)

Subcommittee on
Medical Event Reporting for All Modalities Except for Permanent Implant Brachytherapy

Final Report
April 27, 2017

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Charge to subcommittee: To propose the appropriate criteria for medical event (ME) reporting for events other than permanent implant brachytherapy.

Subcommittee Process

The subcommittee and its Chair were appointed by ACMUI Chair, Bruce Thomadsen, at the regularly scheduled ACMUI meeting October 9, 2015. Subcommittee discussions and deliberations were conducted by teleconference on February 17, 2016. Its initial recommendations were presented at the ACMUI meeting on March 17, 2016. Subsequent discussions and deliberations were conducted by teleconference on August 15, 2016. The revised recommendations were presented at the ACMUI meeting on October 16, 2016. Since the ACMUI committee believed that having an agreement state representative was important, Frank Costello was added to the subcommittee and Pat Zanzonico was removed at the last ACMUI meeting. Most recently, the subcommittee had additional discussions and deliberations on February 28, 2017. This report summarizes the subcommittee's recommendations, which will be presented on April 27, 2017 to the NRC commissioners.

Summary of subcommittee recommendations

- Use proposed definitions for permanent implant brachytherapy that have been reviewed and submitted by the ACMUI.

- Continue to use 10 CFR35.3045 as written for medical event reporting and notification for all modalities except permanent implant brachytherapy.

- Continue ongoing discussion of whether patient intervention should be considered a medical event.

- Encourage major societies to issue a white paper(s) to develop consensus on what should be incorporated into a written directive for various diagnostic and therapeutic modalities.

Introduction

The safe delivery of diagnostic imaging procedures and therapeutic radiation treatments is the highest priority for caregivers, medical institutions, various agencies, and, ultimately, the patient. Given the many advances in imaging, nuclear medicine, and radiation oncology, various radiation modalities are now used to safely and effectively diagnose and treat cancers in addition to other diseases including non-cancerous tumors and thyroid conditions. Radiation therapy, which is a clinically and technologically complex field, can be a very effective primary, adjunctive or palliative treatment, and has been shown to eradicate cancer, control cancer growth, and palliate symptoms such as pain[1]. Since the use of radiation is not without risk and can result in potential harm, the NRC plays an important regulatory role in the medical uses of radiation.

The NRC requires extensive training requirements for physicians who use radioactive materials or byproducts, such as those used in Gamma Knife radiosurgery, brachytherapy, radiopharmaceuticals, and other forms of radiation. Although proper training is one component of safe and effective delivery of radiation for diagnostic or therapeutic uses, the treatment team needs to adopt a culture of safety and quality with checks and balances at every level to ensure that the safest procedure or treatment is being delivered to patients. Since the NRC issues regulations on the medical uses of isotopes, the balance between protecting the public's safety and facilitating the practice of medicine can be difficult to maintain. Given the approximately 7,000 medical licensees between the NRC and Agreement States, any change in medical event reporting can positively or negatively influence caregivers, medical institutions, patients, and the public. It is important that any change in reporting requirements will not restrict patients' access to medical care.

Medical event reporting has not significantly changed over the past 15 years. Aside from some administrative changes in 10 CFR Part 35, Subpart M – Reports § 35.3045 report [68 FR 58805, Oct. 10, 2003] and notification of a medical event [76 FR 72085, Nov. 22, 2011], there has been little change aside from the proposed permanent implant brachytherapy. Various organizations including the American Society for Radiation Oncology (ASTRO) and the American Association of Physicists in Medicine (AAPM) sponsor the Radiation Oncology Incident Learning System® (RO-ILS) to support patient safety of medical procedures using radiation[2].

The delivery of safe diagnostic and therapeutic radiation that utilizes radioactive materials or byproducts requires a concerted effort of the entire treatment team, including the authorized user. Based on an analysis of radiation therapy medical events which included linear accelerators during 2001-2009 in New York, failure to follow existing policies and procedures contributed to

63.6% of events, inadequate policy and procedures contributed to 15.4% of events, and documentation/communication issues contributed to 23.2% of reported events[3]. In a high reliability organization, which is the goal of every medical center, the objective is to deliver the appropriate treatment to the correct patient as safely as possible[4]. Given the evolution of radiation modalities over the past decade, the appropriate criteria for medical event reporting for events other than permanent implant brachytherapy was examined by the subcommittee.

Background

Using the current definition for medical events for all modalities, the number of medical events is extremely low when viewed in light of the estimated 15,000,000 diagnostic and 150,000 therapeutic procedures performed annually. Unfortunately, medical event reporting has come to be viewed by some as punitive, particularly among providers at those medical centers where medical event reporting is scrutinized by many individuals and/or committees with limited or no knowledge of radiation. In addition to the intense scrutiny, medical event reporting dictates a sense of urgency: expeditious notification by the next calendar day and submission of a written report within 15 days after discovery of the medical event. In addition to timely notification of government agencies, the licensee must notify the referring physician and to the individual who is the subject of the medical event no later than 24 hours after its discovery unless based on medical judgment, informing the individual would be harmful. If the referring physician or the affected individual cannot be reached within 24 hours, the licensee shall notify the individual as soon as possible thereafter. This medical event reporting process places culpability on the licensee even if the event may have minimal or no medical consequence.

The table below summarizes medical event reporting for FY 2013-2015 based on the medical events reported at the Oct 6, 2016 ACMUI meeting.

	FY 2013	FY 2014	FY 2015
35.200			4
35.300			7
35.400	16	5	7
35.600	9	11	14
35.1000	15	26	14

Some questions regarding medical event reporting:

1) Do these reports accurately reflect the true number of medical events if the current definition is ambiguous?
2) Should the definition of medical event be revised and updated to reflect the advancements made in radiation delivery, with respect to both potential and actual harm?

3) Does the current reporting process, which is perceived as being punitive by some, impede the desired goal of transparency, education, and adoption of best practices?
4) Does the current reporting process promulgate the lessons learned after root cause analysis from any medical event or does it focus blame on the individual responsible for the event?
5) Should the model of medical event reporting be more aligned with that of the aviation industry which has a spectacular record of quality and safety?

Guiding principles

Since accurate medical event reporting requires transparency and understanding of what constitutes a medical event, the subcommittee believes that any modification to the current definition needs to be carefully considered.

Medical event reporting should allow for the identification of a medical event and provide a forum to discuss how to avoid or reduce the likelihood of such an event. By fostering a just culture of quality and safety, a meaningful root cause analysis will occur serving to decrease the likelihood of such an event through the development of best practices. Furthermore, the definition of a medical event needs to be broad, simple and consistent. If the definition is too complex or is ambiguous, the reports will not be easily applicable to the authorized user, evaluable by regulators or process-focused. Any change in the medical event definition should accurately capture those cases which may cause serious injury or harm to the patient.

The subcommittee believes that any proposed change should not be overly prescriptive and must not encroach on the practice of medicine, which is rapidly evolving. Overly prescriptive changes may inhibit a physician from providing a certain diagnostic or therapeutic modality given concerns for potential medical event (as presently defined) and the subsequent reporting of same, thereby depriving a patient of an available treatment.

The focus of medical event reporting should be on education and improvement rather than punitive action. Some members of the ACMUI subcommittee have reached out to their respective professional societies to increase dialogue about the NRC's role in regulating medical isotopes, in particular trainees whose understanding can be very limited about medical event reporting. By increasing this dialogue, it is anticipated that medical event reporting will serve to optimize patient care through learning and adopting best practices**.**

Medical Event (ME) criteria for a variety of treatment modalities

Given the advances in diagnostic and therapeutic modalities using radiation, medical event reporting needs to address a number of different treatment modalities including:

1) Selective Internal Radiation Therapy (SIRT), e.g. Y-90
2) High dose rate (HDR) brachytherapy
3) Gamma Knife

4) ViewRay
5) LDR implants (non-prostate)
6) LDR meshes
7) Unsealed sources

The subcommittee considered defining ME based on a particular treatment modality in order to make it easier for licensees to determine whether an ME had occurred. Defining ME by modality may make it easier to inspect and regulate and facilitate programs, procedures, and education, which may prevent future events. Although the different modalities of imaging and therapy may have specific inherent risks associated with its delivery, a modality-specific ME for each modality was not favored by the subcommittee as this deviated from the guiding principle of keeping the definition of a medical event to be broad, simple and consistent.

Another consideration was the creation of subsections within the current definition of ME reporting to address the newer, highly conformal radiation oncology modalities that prescribe doses to volumes rather than to a treatment site. With modern radiation oncology techniques and delivery systems, a slight spatial shift of dose can result in significant dose to nearby tissues or parts of organs, which may have medical implications. Since there is variation among authorized users of what constitutes a treatment site within a radiation prescription, the same spatial shifts of dose may have different implications regarding an ME. As an example, some authorized users may use different margins for treatment planning (1 cm versus 2 cm), which would influence how much of the treatment site received prescribed dose. As a result, the subcommittee also did not favor this approach.

Current ME criteria

The current ME reporting criteria under 10 CFR 35.3045 [68 FR 58805, Oct. 10, 2003; 76 FR 72085, Nov. 22, 2011]

(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 percent or more;
(ii) The total dosage delivered differs from the prescribed dosage by 20 percent or more or falls outside the prescribed dosage range; or
(iii) The fractionated dose delivered differs from the prescribed dose, for a single fraction, by 50 percent or more.

(2) A dose that exceeds 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 from any of the following—

(i) An administration of a wrong radioactive drug containing byproduct material;

(ii) An administration of a radioactive drug containing byproduct material by the wrong route of administration;
(iii) An administration of a dose or dosage to the wrong individual or human research subject;
(iv) An administration of a dose or dosage delivered by the wrong mode of treatment; or
(v) A leaking sealed source.

(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 percent 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).

(b) A licensee shall report any event resulting from intervention of a patient or human research subject in which the administration of byproduct material or radiation from byproduct material results or will result in unintended permanent functional damage to an organ or a physiological system, as determined by a physician.

(c) The licensee shall notify by telephone the NRC Operations Center no later than the next calendar day after discovery of the medical event.

The subcommittee believes that the following are clear ME:

(i) An administration of a wrong radioactive drug containing byproduct material;
(ii) An administration of a radioactive drug containing byproduct material by the wrong route of administration;
(iii) An administration of a dose or dosage to the wrong individual or human research subject;
(iv) An administration of a dose or dosage delivered by the wrong mode of treatment; or
(v) A leaking sealed source.

Two areas of the current ME criteria discussed in detail as to whether modifications should be considered were the following:

1) Use of the term 'treatment site' in the definition of ME reporting.
2) Intervention of a patient or human research subject in which the administration of byproduct material or radiation from byproduct material results or will result in unintended permanent functional damage to an organ or a physiological system, as determined by a physician.

Treatment site

Treatment site is defined by 10 CFR 35.2 as "the anatomical description of the tissue intended to receive a radiation dose, as written in the written directive". Some members of the subcommittee felt that the use of target volume or target site rather than treatment site was more consistent with modern nomenclature used, in particular radiation oncology. CT, PET, and MRI

scans are used to help delineate targets and normal structures. Routinely, the concepts developed from ICRU Report 50[5] and 63[6] to help create gross target volume (GTV), clinical target volume, and planning target volume (PTV) for radiation oncology treatment planning for photons and electrons. Since the current definition of ME does not incorporate volume, this may lead to ambiguity about ME reporting. For example, in the case of trigeminal neuralgia radiosurgery treatment, if only a small portion of the trigeminal nerve received prescription dose, would this be a medical event?

However, use of terms like PTV and GTV would be problematic since there is not even agreement among practitioners within an institution and clinical trials as to what constitutes ideal treatment volumes

Since the current 10 CFR 35.2 allows the authorized user to define the anatomical description and the written directive, it allows the authorized user great flexibility. For instance, the anatomical description in the written directive can be described as a treatment volume. Requiring the use of these terms with the incorporation of a minimum volume coverage threshold (GTV, CTV, and PTV) covered by the prescribed dose was discussed as an alternative ME definition, but was rejected giving the difficulty in defining this among subcommittee members. In fact, the American Association of Physicists in Medicine (AAPM) formed task group (TG263) in July 2014 to develop standardization and consistency in naming of organs and structures, dose volume histogram constraints, and other parameters[7]. Nomenclature names were more straightforward to develop for normal organs compared to targets, which is being developed. As a result, in keeping with the principle that medical event reporting should be broad, simple and consistent, the subcommittee supports the use of treatment site with the caveat that societies be encouraged to issue white paper(s) on what should be treated into a written directive for diagnostic and therapeutic modalities.

Since 10 CFR 35.2 relies on the written directive to describe the treatment site and is used to determine if an ME has occurred, it is important that the written directive contains the necessary information for the staff administering the treatment to know how and where the radiation should be given to satisfy the regulatory requirements. Since authorized users at similar facilities may have different ways to describe the same treatment site, it is important that the respective facilities understand the written directive and delivers the administration per the physician's instruction. The written directive documentation needs to contain sufficient information for regulators to determine if a medical event has occurred in accordance with the applicable regulations.

A recent paper by Evans, which was supported by multiple societies, is an example of a white paper on recommendations for the standardization of several key components of the radiation therapy prescription to facilitate accurate communication among radiation caregivers[8]. The key elements for the prescription for radiation therapy and brachytherapy are include treatment site, method of delivery, dose per fraction, total number of fractions, and total dose. They also make other recommendations such as the use of cGy rather than Gy and minimizing the use of decimal points. Development of white papers focused on the written directive would help with the standardization and be educational for authorized users, medical personnel dealing with radiation, and regulators.

Intervention of a patient or human research subject

Even with the most experienced and well trained authorized user and departmental safeguards, intervention by patient or research subject cannot be avoided. As a result, the subcommittee believes that additional discussions are needed about this section of current ME definition. Another subcommittee is reviewing whether intervention by patient or research subject should be reclassified based on passive versus active intervention.

Summary:

Subcommittee on Medical Event Reporting for All Modalities Except for Permanent Implant Brachytherapy recommends that:

- The new definitions for permanent implant brachytherapy that have been reviewed and submitted by the ACMUI should be finalized as rule making.

- The current 10 CFR 35.3045 regulations for medical event reporting for all modalities except permanent implant brachytherapy, does not require a change at this time.

- Discussion should continue on whether patient intervention should be considered a medical event.

- Major societies are encouraged to issue a white paper(s) to develop consensus on what should be incorporated into a written directive for various diagnostic and therapeutic modalities. The benefits of a white paper include 1) help with inspection and regulations by promoting standardization for identifying ME, 2) assist licensees to determine if a medical that has occurred, and 3) assist institutions in developing best practices such as development of standard operating procedures with the goal of preventing future medical events.

Ideally, medical event reporting would allow the licensee to determine if a medical event occurred, would allow the regulator to inspect and regulate, would not encroach on the practice of medicine, and would facilitate educational programs to prevent future occurrences. It is important that the process of medical event reporting fosters a culture of safety and quality with checks and balances at every level to ensure that the safest and most effective care is delivered to patients while simultaneously protecting the public. Licensees are encouraged to continue to audit and monitor their programs and adopt best practices including a high reliability system approach[9] to mitigate medical events.

Respectfully submitted, March 27, 2017
Subcommittee on Medical Event Reporting for All Modalities Except for Permanent Implant Brachytherapy, Advisory Committee on the Medical Uses of Isotopes (ACMUI),
Nuclear Regulatory Commission (NRC)

The report was unanimously approved by the ACMUI at its public meeting on
April 27, 2017.

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