PTCOG Report #2

PTCOG Safety Group Report on

Aspects of Safety in Particle Therapy

Version 2

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Abstract

An important goal of particle therapy is to provide a safe and effective treatment taking into account the entire clinical workflow. This report attempts to provide some information to the particle therapy community that will help point the way to introducing proactive quality management and improve the awareness and culture of safety. One way to do this is to de-mystify Risk reduction processes and provide self-help tools for application of the appropriate procedures and mitigations. The process of particle therapy is multifaceted and multi-disciplinary. Different departments may have different workflows and processes, and will therefore need to analyze their specific situations. This PTCOG report may pave the way for a future PTCOG group to centralize particle therapy safety information.

1. Introduction

1.1 Safety in Radiotherapy

It is important to ensure that a Particle Therapy Facility will accomplish the following:

1. Deliver a safe treatment;
2. Delivery an accurate treatment for effective results;
3. Promote a culture of safety; and
4. Provide a safe environment for all personnel.

The journey starts with the department activities leading up to defining the processes and parameters that will be used to treat a patient and continues with those parameters being delivered by the equipment. For the most part the processes followed are the responsibility of the radiotherapy department and the hardware implemented is the responsibility of the equipment manufacturer whose parameters are then periodically verified by the establishment of Quality Assurance (QA) programs at the facility. This has been the status quo for decades in the field of radiotherapy. However, more recently, and further motivated in no small part by the New York Times articles of a few years ago [1] and incidents in other countries [2], the question of who should be responsible for what processes, and what processes in addition to the equipment QA should be included to enhance safety, have been called into question. Despite the fact that the incidents reported in these articles are the exception that proves the rule that radiotherapy is and has been very safe, it shows that there could be room for improvement.

Moreover, after the first publication of the ISO 9000 standard related to Quality Management Systems (QMS) in 1987 and its widespread use in many different areas of industry and science, the idea of a more general, proactive approach to quality management, including quality assurance and Risk management, has been introduced gradually into radiotherapy. Based on the ISO 9000 series, an international standard for QMS of medical devices has been established by ISO [3]. This can serve as a guideline, when setting up a quality management system. Furthermore, in some countries dedicated standards for QMS in radiotherapy exist, like the German standard “Quality management system in medical radiology – Part 1: Radiotherapy”, published in 2009.

At a meeting called by the FDA[4] to garner input related to the existing situation defined by the NY Times articles [1] , it was clear that the roles of the equipment manufacturer and the facility personnel were effectively being reexamined. For example, one panelist stated that "it is never the fault of the Hospital staff member, it is the fault of the equipment manufacturer". Another panelist noted that the equipment manufacturer should do a better job in training the Hospital personnel about the safety of the equipment. Although it was not clearly stated at that meeting, it seems clear to some that a safe environment and a safe system comes about through a process of managing that safety. This includes understanding what is at Risk, how the Risk is mitigated and a clear identification of the roles of the equipment and the individuals in the processes of radiotherapy.

It is not the case that there is one clear standard to implement safety in radiotherapy. Different facilities follow different workflows; different equipment manufacturers implement checks and/or mitigations in different ways, owing to differences in their equipment (or other reasons). Personnel protocols are as much a part of safety management as hardware and software interlocks. One could argue that this is due to a lack of standards, but another viewpoint is that it is due to the diversity in a continuously growing field.

Even if it were possible to implement all safety protocols within the equipment, would that be the appropriate thing to do – taking the human out of the equation? It is the case that radiotherapy these days is becoming more and more complex. Human intervention may not be possible in time to prevent injury during the beam delivery part, but the degree to which this can be designed is still open.

In particle therapy equipment systems, a special problem may be that not many identical systems exist yet and very often additional in-house products are combined with commercial systems. This can result in modifications to standard radiotherapy processes and from a hardware perspective it could result in interface compatibility challenges. In such a specific situation there must be a clear responsibility for analyzing the Risks of these systems, including the interfaces. Certified components will generally have very clearly labeled interface specifications. However particle therapy has many processes in common with conventional radiotherapy, whose safe implementation should also be addressed.

1.2 Goal and flow of this report

The goal of this report is to provide some of the information and tools needed to do a self-evaluation of processes and help in the implementation of safety. The philosophy is that the more engaged the staff is in the creation of a culture of safety and in the understanding of how safety is implemented, the safer the environment will be. Creating a culture of safety is not simply being careful and watching out for accidents or retrospectively discussing specific issues, it encompasses elements of understanding systems and contributing to the proactive quality management methodologies employed in a department.

Some think that doing this is too hard. It is not. In order to accomplish this goal it seems useful to identify ways in which safety management is implemented generally, but also to provide specific tools which can be used to analyze possible safety concerns in a specific facility and determine whether the mitigations that are necessary have been appropriately implemented. This is not to say that the full Hazard Analysis for the equipment performed by an equipment manufacturer must be reproduced, but it is useful, at least to understand how these can be done, and how it can be extended to other (less technical) aspects of the treatment workflow. For each technique to be described herein, there are multiple ways in which it can be implemented. For the purposes of this report we tend to concentrate

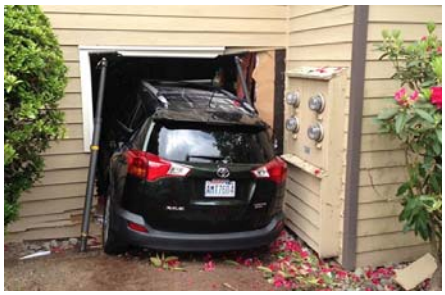
on methods in common practice and provide some examples of alternative approaches. General guidelines for improving the safety in radiotherapy can also be found in the standards published by IAEA [5].

In this report, a description of the main methods to think about and analyze issues that affect safety will be provided along with templates that can be used to help start the reader to create their own analyses. All aspects of technical, human and organizational factors should be considered. The organization of this document is guided by an attempt to introduce and define the inputs required to various forms of safety analyses followed by description and examples of the types of analyses and the resultant outputs. The flow of the contents of this report will be as follows:

- Definitions of Hazard and mitigation.
- The concept of prioritization of the importance of a Hazard by understanding the Risks.
- Models and templates for the evaluation of Hazards, Risks and the effects of failures.
- The types of mitigations that can be applied.
- Elements of patient treatment workflow, to be considered in analyses.
- Aspects of Quality Assurance

Finally, it seems clear that having some way to get information about issues, incidents and other related data from other facilities, that either actually happened, or that has been considered (presented in a useful, anonymous way), can be used to help others to improve their systems to mitigate situations that were previously not considered. For medical devices in general, there exists a mandatory reporting system for adverse events, which can be a valuable source of information. It is found on the FDA's website and is called MAUDE - Manufacturer and User Facility Device Experience [6]. On this site one can search explicitly for adverse events with certain devices of a certain manufacturer. Also the International atomic agency (IAEA) has compiled reports of errors in radiotherapy [7].

2. Introduction to Hazards and Mitigations



As an introduction, it is helpful to identify a number of concepts to keep in mind when setting out to consider how to think about determining if a process is safe and what to do to help it to result in a safe outcome. Before jumping into any analyses, it's useful to discuss the terms and philosophy. First, one can note that a Hazard has various definitions, depending upon the framework of an analysis. A Hazard can be a circumstance which sets up the possibility to cause an unplanned or undesirable event (e.g. a live electric wire on the ground), or sometimes the term Hazard and accident are used synonymously (e.g. someone stepping in water puddling on a floor on which a live wire is lying). When reading about this topic, take care to understand how the terms are used. There are a number of ways in which to cause a Hazard. It can be generated by equipment, by humans and by combinations thereof. Also, there are Hazards which are a result of a primary action (equipment or human), or a Hazard resulting from a reaction to another issue (e.g. pushing the gas instead of the brake when trying to stop a car). It is not believed that one can eliminate all Hazards, but it would be good to have a system that is protected from Hazards. One would institute Mitigations.

One can attempt, as in the photos below to mitigate by:

- Prevention
- Detection
- Reaction

We all live in an environment that we have attempted to keep safe and sometimes we believe we have an intuitive sense of how to implement safety. Even in the photos above, while the use of prevention, detection and reaction are implemented, this doesn't result in 100% success. System and workflows that are more complex require a level of analysis beyond our day-to-day instincts. Some of the questions posed are the frequency of detection and time for reaction. These are just as necessary in a radiotherapy environment.

One may ask whether we can 'prevent' all errors in radiotherapy. From an equipment perspective, take an airplane as an example. Is an airplane prevented from losing altitude, or is a loss in altitude detected and reacted to? In a radiotherapy workflow example, can one prevent the wrong image from being used, or does one do the best one can, but continue to detect and react to this? These are the kinds of questions to be sensitized to while analyzing a given situation. Finally there is the question of whether something should be dealt with by humans or by machine. From an equipment perspective consider the following. Conventional radiotherapy consisted of ~30 fractions per course of treatment with about 1 minute/field. Let's say that human thinking reaction (not instinctual reaction) time is about 3 seconds. 3 seconds out of 1 minute is 5%. Perhaps this is what has led to a one minute treatment, this allows a human to intervene while only a 5% error is made. On the other hand, proton beam spot scanning has a timeframe of milliseconds per spot and while an error analysis is dependent upon dose rate and specific treatment planning issues, one can see that this is below human reaction time. Also, in conventional radiotherapy a 1mm leaf gap results in a 5% dose delivery error, which is also below human detection capability in a clinical treatment scenario. However all leafs open instead of in a particular pattern is well within a humans' capability to detect.

Generally, there exist different ways to mitigate Risks:

- Risk avoidance by design of the equipment, i.e. a failsafe design
- Risk mitigation by quality assurance, e.g. by a daily check or double check
- Risk mitigation by notification, e.g. by informing all personal about a specific measures and training them accordingly

These methods will be further discussed in sections 4-6.

3. Introduction to Risks and Criticality

In the previous section, Hazards and mitigations were defined. Two of the key tools that are used as input in safety analyses are Risk and Criticality. This section covers ways of defining these quantities. According to IEC 601-1-4 and ISO 13489-1, the term Risk is defined as the combination of the probable rate of occurrence of a Hazard and the degree of Severity of harm caused by an accident associated with the Hazard. The result of such an analysis is the importance of the effect and the identification of a mitigation to reduce the Severity and/or Probability of the effect. While there are many methods and references, there is also an ISO standard ISO 14971:2007 [8].

3.1 Hierarchy of Risk Parameters

Again, Risk is a combination of the Severity of a Hazard and the Probability of occurrence of that Hazard. There can be several levels of the Severity of a Hazard. For example is someone subjected to a bare wire from low voltage lawn lighting, or the bare wiring in a 200amp main circuit breaker panel? Generally, in practice, there are 4 (or 5 levels if the no determination category is used) as noted in the table below.

Table 3.1.1 Hierarchy of Severity

Term	Level	Description
Severity	5	No determination has been made yet (assume the worst)
SERIOUS	4	Results in death, permanent impairment or life-threatening injury
MODERATE	3	Results in recoverable injury or impairment requiring professional medical intervention
MINOR	2	Results in recoverable injury or impairment not requiring professional medical intervention
NEGLIGIBLE	1	Inconvenience or temporary discomfort

These levels may be defined differently for different circumstances and may, for example, be reflective of individual or group Risk. For example in the case of radiotherapy, there may be specific dose constraints associated with each of these levels (e.g. section 5.4).

The levels of frequency or occurrence (or Probability) can be defined according to the following table, although different time frames are considered in different circumstances:

Table 3.1.2 Hierarchy of Probability

Term	Level	Description (occurrences in installed base over lifetime)
Probability		No determination has been made yet
UNDETERMINED	U/5	Unknown – i.e., caused by software flaw, misuse or user error. Indeterminate occurrence rates.
FREQUENT	5	A common/typical occurrence. (≥1/year)
PROBABLE	4	Likely to occur several times over the lifetime of the product. (~1/year to 0.1/year)
OCCASIONAL	3	Likely to occur few times over product lifetime. (~.001/year to 0.1/year)
REMOTE	2	Likely to occur at least once during the lifetime of the product but is highly improbable. (<.001/year)
IMPROBABLE	1	Unreasonable to expect occurrence over lifetime of the product but is theoretically possible. (<.00001/year)

In addition sometimes these levels are subdivided further into a total of 10 or more depending upon the individual analyzer's tastes or specific implementation. Note that an undetermined Probability, or Severity may be treated as undefined or as the maximum depending upon the degree of conservatism used in the analysis.

3.2 Categories and Qualifiers of Risk

The combination of Severity and Probability determine, by definition, the Risk Potential Number (RPN). For example in the tables above, the maximum RPN is 20 (=5*4) and the minimum (for those that are defined) is 1. In addition, one sometimes considers how hard it might be to detect an occurrence of a Hazard which essentially modifies the probably rate or frequency of that occurrence. The same is true of a measure of 'avoidability' which is sometimes explicitly included (although is obviously related to detectability). While it is not strictly speaking a separate quantity (in some opinions), it is sometimes separated from the Probability number. Sometimes the RPN is referred to as Criticality and the RPN numbers may be subdivided into Criticality categories. The RPN is then used to inform the analyzer about the necessity of mitigation and type of mitigation (very secure or less secure) to be used to attempt to prevent an accident.

The main goal of this section is to define an RPN that can be used to inform the Hazard or Failure Mode Analysis. One would then use that RPN to determine a mitigation.

Below are various examples of how the RPN can be calculated.

3.2.1 RPN Tree or Risk Graph and Categories

One can simplify (not always appropriate) the analysis of Risk by approximating the Risk number contributions as follows:

Define S1 = Moderate Severity (Less Severe)
Define S2 = Serious Severity (More Severe)
In this example, only S1 and S2 are considered for the Severity of the possible injury. The analyses we describe can be used for all aspects of a system which includes all the steps leading up to and including the treatment of a patient, from consultation through planning and treatment. Therefore, one consideration is that of the radiation dose that will be or is delivered. For example, in cases where inadvertent dose >2Gy is delivered to a critical structure (which could be due to an improperly contoured diagnostic image or a failure of the equipment), these could be considered S2 Severity. In addition, situations in which electrocution or heavy objects falling on people, while not directly related to radiation, may also considered S2 levels of Severity. Drawing the line is still, however somewhat subjective and identifying the above considerations is designed to see if the reader reacts to them and has their own impression of how the rating should be structured.

Define P1 = Includes Occasional and Remote Probability (Lower)
Define P2 = includes Probable and Frequent and Undetermined Probability (Higher)
In the case of Probability, there are a variety of issues to consider. In the case of a falling object, one can consider both the Probability of a device failing (a potential Hazard, a potential accident or a Hazard (depending upon your definition of the word Hazard), but not an accident) or one can consider the Probability of an individual being subjected to the Hazard (e.g. walking under the falling piano at the right moment). For example, it is more likely that a patient directly receiving therapeutic radiation will be in the treatment room when the beam is on than other individuals and therefore the Probability may be different for different categories of person. Considering another issue, for example, is it more likely that a computer will transfer data accurately compared to a human transcribing it?

*Define A1 = High ability to **A**void (and/or Easy to Detect)*
*Define A2 = Very difficult to **A**void (and/or Hard to Detect)*
Again, these quantities include a variety of considerations. As noted above, some consider these to be simply modifiers of Probability and do not address them separately. Indeed there are many aspects of Probability and one cannot address them all separately. This is done here, for the sake of example. When evaluating this quantity for irradiation, one can consider the quantities associated with beam delivery that are measured on-line. Of course, the act of measuring beam quantities on line is, in fact, a safety mitigation determined from the Risk analysis and/or the FMEA (to be discussed below). In this case the act of a mitigation may in fact change the ability to detect or avoid the Hazard. Therefore the mitigation modified the Probability in this case. Another method that can be helpful in avoiding accidents are those activities generally supervised by experienced staff. This will again change the relative Risk depending upon the category of individual involved. An experienced staff member may notice that a certain treatment plan does not match with the patient's disease, if there is a mitigation that the staff member should check it and therefore be able to detect it.

Given these quantities one possibility is the following analysis tree which leads to a way of categorizing the level of the Risk AND determining what type of mitigation should be considered. Given the combination of Severity and Probability (and Avoidance and/or Detectability) one can the value of the RPN to identify a potential Risk category "Criticality" category. Based upon this category, certain action may be warranted. For example the following categorization of mitigation from EN 954-1 is sometimes used:

Table 3.2.1.1 Category Hierarchy Table

Category Number	Implication of Category
1	A safety function implemented should be checked from time to time.
2	Design the system according to well-tested components and safety principles.
3	Design such that one single error does not cause the loss of a redundant safety function and when practical that safety function operation is detected independently or tested, thus minimizing the loss of redundancy.
4	All the above plus design the system so that the error of a component does not cause the loss of the safety function

In the matrix figure 3.2.1.1, below, the numbers across the top row refer to the categories of mitigations identified just above (1 thru 4). The letter/number combination along the side are combinations of S and P and A. For example S1 is low Severity and therefore other qualifiers (probability and avoidability) are not factored in. (This is how it was done in EN 945-1. In the newer ISO 13489-1 the S1 line now subdivides.) The red circles in the cells are the preferred Criticality category(ies) of mitigation (see 1-4 above) for the particular combination of parameters which leads to a given row. For example, the 3rd row is comprised of S2*P1*A2. In that row, one might perhaps implement a lower category (e.g. category 1 - blue circles) if one has good reason to do so and these reasons should be recorded. The preferred category of Risk to evaluation is either 2 or 3 (red circles). One can also implement a higher category (yellow circles) for conservatism or a particular set of reasons. Note that the evaluations are

essentially multiplicative results of the various components with equal weights. Of course this will depend upon how the 'numbers' are assigned to the various issues.

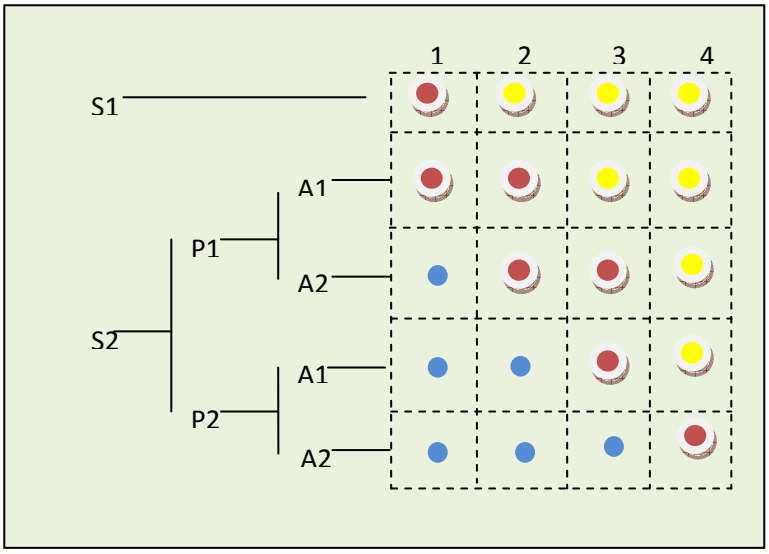


Figure 3.2.1.1 Risk Mitigation Table

3.2.2 Brute Force Calculation

The previous method was particularly rigid and minimized the assignment of Risk and Probability. Although it was a standard, that standard (as noted above) has been updated and there are more gradations. One can perhaps best think of this by allowing a certain degree of flexibility by increasing or decreasing the number of choices of categories and thereby provide additional flexibility in choosing the threshold for a given RPN/Mitigation categories in some situations. Increased choice may also lead to increased difficulty of analysis. One can do this in a simple, brute force way, for example.

If one did a straightforward numerical analysis of 4 categories of Severity, 5 of Probability and 2 of avoidability, the results would be as in table 3.2.2.1 which follows.

A simple product of Severity, Probability and avoidance yields a maximum possible number (called Criticality in this table) of 40. One can then define categories based upon the product. The most serious category (IV) can be defined as those items with a score ranging from 31 to 40 and similarly for lower scores from 21 to 30 can be assigned category III etc. This has a similar format as in the previous figure, but is more straightforward to handle numerically. However it may be considered a bit more subjective in that the analyzer must identify that line separating the categories. One can then assign mitigations based on that category. The colored rows go along with the category listed in the column before Criticality.

Severity	Probability	Avoid		Criticality				
				0	I	II	III	IV
	1	1		1				
		2		2				
	2	1		2				
		2		4				
	3	1		3				
1		2		6				
	4	1		4				
		2		8				
	5	1		5				
		2		10				
	1	1		2				
		2		4				
	2	1		4				
		2		8				
	3	1		6				
2		2	I		12			
	4	1		8				
		2	I		16			
	5	1		10				
		2	I		20			
	1	1		3				
		2		6				
	2	1		6				
		2	I		12			
	3	1		9				
3		2			18			
	4	1			12			
		2	II			24		
	5	1	I		15			
		2	III				30	
	1	1		4				
		2		8				
	2	1		8				
		2	I		16			
	3	1			12			
4		2	II			24		
	4	1	I		16			
		2	IV					32
	5	1	I		20			
		2	IV					40

Table 3.2.2.1. Another (brute force) categorization

3.2.3 Binary Combination

The sections above outline a systematic means of identifying the highest-risk processes, procedures or technology. Once the highest Risk issues are identified, one can start to reduce Risk through safety improvement mitigations. In the simplest form, one might, for example, create a binary structure, basically drawing a line between those Risks that require mitigation and those that do not. As an example, the table below uses the Probability and Severity combination to identify what combinations should be mitigated and which are acceptable Risks. One can replace this table with a threshold in a range of other RPN definitions. As alluded to several times in this report, some accept that only Probability and Severity lead to Risk and that detectability and/or avoidance contribute to the Probability number. Some like to see these additional factors explicitly called out. However your team decides to do this, the point here is that there can be a range of RPN below which no mitigation is necessary and above which it is. Depending upon how much above the RPN is, the type of mitigation may be different. This will be reflected in the Hazard and FME analyses.

Table 3.2.3.1 Binary combination of Probability and Severity

Probability	Severity			
	NEGLIGIBLE	**MINOR**	**MODERATE**	**SERIOUS**
UNDETERMINED	ACCEPTABLE	MITIGATE	MITIGATE	MITIGATE
FREQUENT	ACCEPTABLE	MITIGATE	MITIGATE	MITIGATE
PROBABLE	ACCEPTABLE	ACCEPTABLE	MITIGATE	MITIGATE
OCCASIONAL	ACCEPTABLE	ACCEPTABLE	MITIGATE	MITIGATE
REMOTE	ACCEPTABLE	ACCEPTABLE	ACCEPTABLE	MITIGATE
IMPROBABLE	ACCEPTABLE	ACCEPTABLE	ACCEPTABLE	MITIGATE

For some situations this simple demarcation is inadequate. One can go to the next step and, for example, using Table 3.2.2.1, break out the Risk numbers individually and subdivide the results into an arbitrary number of categories. This table identifies four categories. One standard (EN 954-1) suggests considering these four categories in table 3.2.1.1.

4. Evaluation Models and Methodologies

Over the decades, various methods to analyze accidents have evolved.

4.1 Evaluation Models

In 1931 Heinrich published the "Domino Accident Model" [9] (figure 4.1.1 below to the left) which is based upon the postulate that once you set a chain of events in motion the result is inevitable. It is a linear chain of events and removing any one domino has the possibility to stop the chain. The elements of the chain include social environment, carelessness, and action. This model was used in the early 20th Century when factories and people were a main source of accidents. Reason proposed the "Swiss Cheese Model" [10] (below right figure 4.1.1) of system failure. It is an evolution from the Domino model in that it incorporates multiple possible sources of error (the holes in the Swiss cheese). Each hole in the Swiss cheese represents an opportunity for a process to fail. While it is also a linear progression, the only way for an accident to occur is for the holes in each line of defense to line up.

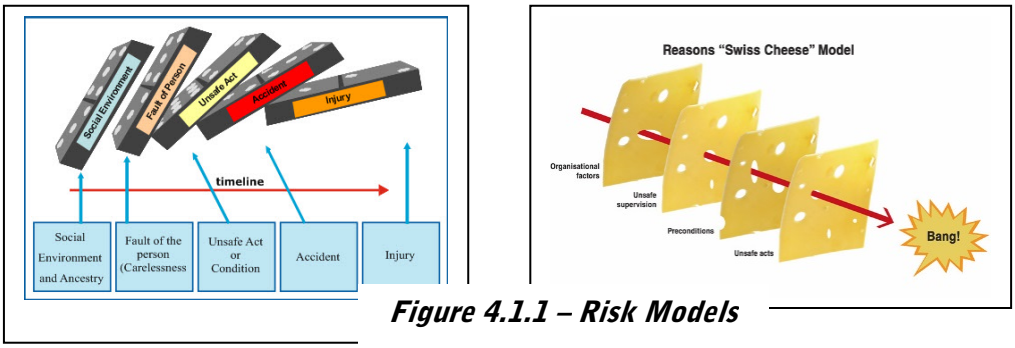
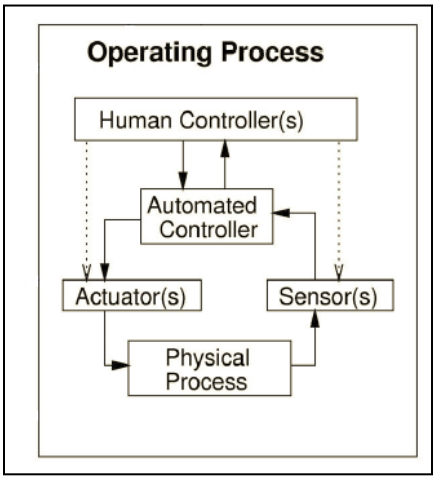


Figure 4.1.1 – Risk Models

(Note that even these early models incorporate multiple lines of defense or multiple steps to an end.) Which holes are in which position may be random; alternatively, the location of the holes at any given time may be random. Note that this model is from the mid-20th century and still includes organizational factors such as supervision as prerequisites for accidents. The fact that there are multiple holes may allow for the possibility that various factory processes may come into play. Both of these models incorporate management, social culture and environment. The fact that these are older models does not mean that these factors should be ignored in a modern day analysis. Some models even incorporate input from government interactions, or in a case such as radiotherapy, the guidelines and reports of such organizations as AAPM and FDA, or IAEA and ISO on an international level, as these may play a role in Hazards as well.

With modernization comes increasing complexity and the need for more complex analysis models. One such model is the Functional Resonance Accident Model (FRAM) [11] which postulates that even from random noise, circumstances can conspire to cause a coherent looking signal. In other words a system can be so complex that it may be impossible to identify all the 'Swiss cheese holes" and there will be some finite possibility that they will align at some time.



Finally, a more recent development is the System Theoretic Accident Model and Process (STAMP) [12], published by Leveson. The central assumption is that the nature of technology has evolved to form very complex socio-technological systems. Among the concepts which this model wishes to explicitly incorporate are the interactions between sub-systems and possible failures of mitigations. According to STAMP, the analyst will first prepare a control diagram of the system in question in order to identify which control actions exist such as in the diagram on the right. This is effectively a diagram which incorporates processes and mitigations and the criteria for the operation of these loops and failure modes are itemized. For any process there are decisions made based upon data and there are potential errors in this. In this model, not only can a component failure or a control action not being executed cause an accident but there may be subtleties in the timing of a control action which may be inappropriate for the desired mitigation. While within the original STAMP process no further quantification is recommended, many users have combined the methodology with various Risk quantification methods in practice.

How one analyzes a given set of processes and/or systems may, at this point be individualized, to some extent. The authors of this report emphasize that, for any analysis style, taking into account the appropriate possible issues that can arise is the most critical aspect. No system automatically provides all the inputs, outputs and interrelationships necessary to perform an analysis. It is up to the analyzer to incorporate the necessary data, ask the appropriate questions and go to the appropriate level of detail to optimize the safety of a system. The process of incorporating appropriate data can be facilitated by many mechanisms including a safety culture that encourages robust reporting.

In virtually all these processes the following should be identified:

- Requirements for effective system performance
- Processes that are needed to fulfill those requirements
- Hazards that can arise in the execution of these processes
- Methods to mitigate either the cause of or result of the Hazard, including failures of the mitigation

The analysis may be different for a system currently under design and one already in operation depending upon the amount of information available. Reverse engineering a system is at best a problematic endeavor, but if it is a process which a staff lives daily, without hidden actions, then there is a high likelihood of being able to identify all the requirements and processes.

Having identified the types of accident models and key elements required for Hazard analyses, it is useful to briefly summarize some analysis tools which will be discussed in more detail later. The above models are primarily models to help one think about the problem, with the exception of STAMP which includes analytical methods as well.

Typically the following three “tools” are used to analyze system safety.

- Fault Tree Analysis (Hazard/Risk Analysis)
- Event Tree Analysis
- Failure Mode and Effects Analysis (FMEA/FMECA)

A Fault tree analysis is a “TOP DOWN APPROACH”. One identifies a chain of events starting with an accident or Hazard or fault, identifying what Hazards may contribute to that accident. One then classifies the importance of that Hazard, identifies the causes of the Hazard, and figures out mitigations to deal with these causes and Hazards. One might start with a system that has or has not included mitigations, designing a new system or reverse engineering a system. Typically a system and/or workflow is separated into many smaller components or steps and each component is the analyzed separately for a given Hazard. In a particle radiotherapy unit, these components may include aspects of treatment planning, oncology information system and building infrastructure. In addition technical factors may be considered including such details as: ion sources, main accelerator, beam extraction system, beam delivery, monitoring system, control system, power supplies, patient positioning devices, imaging devices, etc. as all possibly contributing to the same Hazard. This method has proven to be so effective, that only complex (sometimes referred to as ‘nonlinear’) interactions are left as sources of error.

An Event Tree Analysis starts with, for example, a failure event and a mitigation of that event or a

mitigation of the effect of that failure and the analysis then walks down the path of those issues that can prevent that safety mitigation from working.

A Failure Mode and Effects Analysis is a "BOTTOMS UP APPROACH". One evaluates, for a given process or subsystem a particular action or component and identifies how a failure of that item might contribute to an accident. One classifies that effect and identifies a mitigation for each error case including errors in the mitigation itself. In this case, one is starting from an arbitrarily low level of components or steps and imagines if that component of step errs, what would be the result and would that result affect safety or even accuracy. This is often confused with a Hazard analysis, which starts with a Hazard and figures out what component caused it (if followed that far), as opposed to starting from a component and figuring out what accidents can arise from an error. This may even be confused in some literature. The reader is cautioned to read carefully.

These tools help to either visualize (if drawn graphically) or at least articulate a clear systematic approach to identifying potential system issues. Note that in the analyses described above, terms like identifying a failure are used. One of the important things that is not so deeply understood, is that this is not just a failure of a component (e.g. resistor), or step (lost prescription), this could also be a failure of a 'control action' which was performed based upon some input. Some of the newer methods, such as STAMP explicitly identify these types of issues, but does not find these issues automatically. None of the other schemes preclude inclusion of these types of issues. It is a subjective statement to say that such situations can also be incorporated in these 3 tools and are generally performed by experienced individuals. There is no system that finds inputs not given by the analyzer. There are however attempts to more easily capture the manually entered system requirements and dependencies and this assists in the analysis.

In the end, if a system is too complex, it is difficult to convince oneself, or anyone, that the appropriate set of mitigations have been properly implemented. It is therefore necessary not only to implement Risk mitigation strategies, but also strategies to verify, that these mitigations actually work. This type of verification of Risk mitigation is an essential part of the procedure. *One should try to be simple and to design a system that can be understood if possible*. One way to do it is to separate functionality, although interfaces then have to be addressed.

Finally, it is necessary to define a safe state. Note that the ABSENSE OF TREATMENT is not necessarily a safe state, since lack of treatment can lead to negative consequences. One should have such a safe state to enable (if possible) some time to consider what to do next before cancelling a treatment.

4.2 Risk Assessment in Healthcare

Before studying the details, however, it is useful to briefly consider the history of risk analysis in the context of healthcare. In about 3200 BCE a group called the Asipu lived. They served as consultants for helping to make decisions. They would identify the important issues and alternatives and evaluate whether an alternative was positive or negative and recommend a course of action. This may have been the first form of risk analysis. When science evolved to the point of having mathematical theories of probability and causal links (e.g. Halley 1693), formal Risk analysis become possible. Casual relationships in medicine are much more recent as in the work of Pasteur in the 19th century.

The Hazard Analysis (e.g. Hazard Analysis and Critical Control Points) and the Failure Modes and Effects Analysis (and Failure Modes and Effects Criticality Analysis) were first developed for the military; the former for artillery shell firing mechanisms and the latter where it was employed by the Navy in the late 1940s. Later the methodology was taken up by NASA in various forms, and by the 1970s had made its

way into food processing and manufacturing and other arenas where it is now widely used. Of particular relevance for healthcare is the fact that since 1990 the FDA requires device manufacturers to conduct a prospective Risk assessment as part of the Medical Device Good Manufacturing Practices Regulations. This requirement is often fulfilled with an FMEA.

In clinical operations FMEA, or variants have been used in a variety of disciplines including anesthesiology, nursing and other areas. It is sometimes the case that, in healthcare, the distinction between an Hazard Analysis and an FMEA are not well separated, so take care in reading discussions about this. The Risk analysis is a recognized tool by The Joint Commission (TJC) which accredited nearly 20,000 healthcare organizations in the US. In 2001, TJC issued rules (Rule LD5.2) requiring organizations to "At least annually, select at least one high-risk process for proactive Risk assessment" [13]. This is often conducted via FMEA. TJC publishes an excellent practical book on the use of FMEA within healthcare [14].

The use of FMEA in radiation oncology (outside of its use in machine design) is relatively more recent. In 2009 one of us (EF) published the first report of FMEA in a radiation oncology clinic, a technique that the group was guided in by experts at the Johns Hopkins School of Public Health [15]. A number of studies have appeared in the years since including application to stereotactic body radiotherapy [16], MLC tracking systems [17] and other clinical applications. FMEA is also the subject of an upcoming Task Group report within AAPM. TG-100 was formed in 2003 with the task of revamping Quality Assurance needs for radiation oncology. The TG-100 report, approved by AAPM and due out in 2016, will focus largely on FMEA [18]. At the international level within radiation oncology, ICRP Publication 112 describes FMEA and advocates its use in Risk reduction programs [19].

It may be helpful to note, that at least one author believes that there is still sometimes confusion between the Hazard analysis and an FMEA. One may distinguish by noting the direction of the analysis. Does it start with a Hazard and ask how that could be created, or does it start with a step or component and ask what could go wrong and what would that do? The former is a Hazard analysis, and the latter is an FMEA. What counts, however, is whether one or the other, or a combination can be used to maximize the possibility of identifying those mitigations necessary to achieve a highly safe system.

5. Hazard Analysis

The Hazard Analysis [8] is a comprehensive process that is intended to analyze all foreseen Hazards that can occur as a result of the system workflow and operation. The goal of a Hazard analysis is to identify conditions which would give rise to a given Hazard and prioritize them for possible safety improvements. A key output of this analysis is the determination of the biggest Risks and possible mitigations.

An analysis of this sort requires inputs and generates outputs. Identifying and assembling the inputs is critical to the success of the analysis. Asking the appropriate questions, together with the completeness of the input, helps to generate the most complete output.

A Hazard Analysis (also called a Risk Analysis or sometimes a Fault tree analysis [20] (not to be confused with a Failure Mode and Effects Analysis (FMEA))) is a "TOP-DOWN" process. Briefly the following steps are to be performed:

1. Pick a Hazard
2. Identify a Subsystem

3. Imaging how that Subsystem can cause that Hazard
4. Score the importance of that Hazard
5. Create a Mitigation
6. Identify how that Mitigation will be verified (Is a mitigation a real mitigation if you don't know whether or not it is working?)

In the normal flow of the Hazard analysis, it very quickly gets to the point of identifying sub-steps and how these can cause the Hazard being considered. In general, the Hazard Analysis will be maintained at a higher level, and may go down to a subsystem level but not at the component level or below a sub process level which will be dealt with in a more detailed "BOTTOM-UP" FMEA analysis.

5.1 Hazard or Accident Identification

Such analyses require inputs and yield outputs. One input is the identification of a Hazard. While it is unlikely to identify every single possible Hazard or every possible error condition which may arise, it is the expectation that, through a careful and systematic evaluation of the types of Hazards identified in ISO 14971 and 21 CFR 820.30(g), and in conjunction with other techniques (e.g. FMEA) it will be possible to achieve an acceptably safe system. One example of a list of Hazards is shown in Appendix C from prEN 1441. Thus, an input to the Hazard analysis includes a list of the types of Hazards to be considered. Hazards which may affect the health and safety of patients, staff and visitors are to be considered. In addition, there may be multiple effects of a Hazard. Sometimes the accident caused by the Hazard should be considered.

5.2 Subsystem Identification

Another input is a list of the 'things' that may cause the Hazard under consideration. One of the subjective elements in the performance of a Hazard analysis is the selection of which items to include in this analysis including the list of the components of the system (including human or equipment steps) which must be analyzed.

It should be reemphasized that the analyses being discussed can be applied to the entire radiotherapy clinical workflow. Just one element of that is the equipment related Hazards. Thus a 'component' can be a step of the workflow. However the equipment related Hazards are such a rich source of possibilities, that it may be helpful to highlight these.

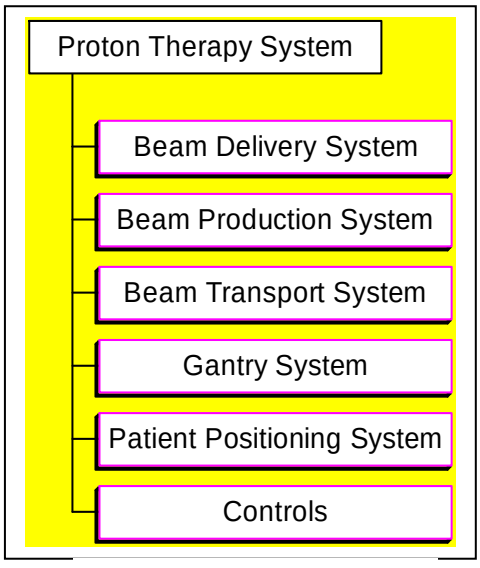


Fig 5.2.1 Subsystems

Figure 5.2.1 to the right shows a breakdown at a high level of the subsystems that comprise a typical proton therapy system. When one is considering a particular Hazard, one can include each of these subsystems. The trick is to identify the 'requirements' of each of these subsystems to enable a breakdown of the possible errors, or deviations from requirements, that may result from these subsystems. Indeed one may find that a particular requirement hasn't been considered, which would be needed to avoid or mitigate a Hazard. For example, a gantry structure (not including the beamline which is part of the beam transport system) affects the beam angle but not the beam energy, so Hazards associated with the beam range in the patient may not be affected by the gantry. On the other hand, a gantry's motion may

affect the alignment of the beam transport elements which may, in turn, affect the beam properties such as beam position. The success of a Hazard analysis will partly be determined by how well one highlights the subsystem requirements and/or functional decomposition.

In addition, a mis-administration of irradiation can be caused by an incorrect CT image which was used for treatment planning. That incorrect image can be a result of the subsystems that dealt with that image including, but not limited to:

- Computer data transfer
- Incorrect name placed by a technician
- Incorrect import to the TPS
- Incorrect contouring

It is perhaps a good use of the 'Use Case' representation, given all the 'actors' involved to analyze this situation, which is a way to break down the steps and identify how different users interact with them,, although the results are analogous with an equipment decomposition. The question is which is the best representation to help analyze the situation?

Once one has accumulated the subsystems and steps and actors and their respective responsibilities and requirements, one then can ask how the particular Hazard being identified may be caused.

5.3 Hazard Analysis Examples

5.3.1 Hazard Table

A helpful tool or visual representation to aid in the analysis of Hazards is a table. The table helps to ensure that the relevant information is captured and the appropriate questions are asked. The table does NOT help to ensure that all the causes are found.

To further illustrate the development of a Hazard analysis consider a simple practical example from outside of healthcare. Imagine that you are an official with the National Highway Traffic Safety Administration in the early 1970s. You are tasked with performing a comprehensive assessment of automobile safety. Like the use of a Hazard analysis in healthcare, the first and arguably most crucial aspect of this exercise is to identify the inputs and develop a comprehensive list of relevant Hazards. You might consult consumer safety reports or solicit input from manufacturers or conduct targeted interviews with experts on the topic. The broad goal is to develop the most comprehensive list possible. You know the list will be long, but the Hazard analysis formalism will provide a manageable prioritization in the end. Table 5.3.1 presents a hypothetical sample list.

Table 5.3.1 Automotive Hazard Analysis Example

	Hazard	**Cause**	***S***	***P***	***D***	***RPN***
1.1	Car will not start	Dead battery	1	5	1	5
1.2	Car will not start	No gas	1	5	1	5
1.3	Car will not start	Electrical short	1	1	1	1
2.1	Tire flat	Puncture	5	5	1	25
3.1	Bad Collision/Personnel	Speeding on a dark road	10	5	1	50
3.2	Collision/Moderate Damage	Back up into something	5	5	5	125

(Table 5.3.1: Example failure modes and RPN component scores for a hypothetical exercise in improving automobile safety. The scores for Severity, S, Probability of occurrence, P, and detectability, D, which are multiplied to compute a Risk priority number, RPN=S×P×D.)
Once the Hazards have been identified, one tries to provide additional inputs and identify possible relevant causes, in this case by examining components and actions and actors. (Note in this case that an actor can be a driver or a nail in the road.) Of note, in this table, is the fact that some Hazards may have multiple causes. For example "car will not start" could be caused by a dead battery, an empty gas tank, or an electrical short (in addition to many other causes not listed). When there are multiple causes for a given Hazard, it is helpful to separate out these causes since the scores may be different. However, in a Hazard analysis it is not always necessary to drill down to the most detailed causes. What may be surprising in this table is that the RPN for the last row is higher than the RPN for the next to the last row. That is because it should be easier to detect that the car is speeding, than to know what is behind the car. Of course this would change if there was a back-up camera, or if in the former case, the driver were intoxicated.

5.3.2 Root Cause Analysis

As mentioned earlier, one of the areas of subjectivity is the level of detail that is investigated in this analysis. In this regard, table 5.3.1 represents a somewhat deficient analysis. Some of this has already been intimated above. The Hazards and/or causes listed are not very specific. One tool to help one identify the causes of a Hazard is the Root Case Analysis (RCA). Depending upon the experience of the group involved it could be that performing these analyses involves an intensive often weeks- or moths-long effort to understand causal factors. RCA is widely used in healthcare [21], though it is most often deployed in the wake of a serious misadministration. Hence the term "Root Cause", which implies finding the cause of a specific issue. Nevertheless, its general goal is applicable to any safety mitigation: to identify all of the relevant causal factors, of which there is nearly always more than one. Taking the example of automobile safety in table 5.3.1, we see that the failure mode with the highest Risk priority number was a collision resulting from backing up into something. It would be an assumption at a certain level to take this failure mode information alone as a basis for safety mitigation. Depending upon the situation, much more detail is needed as to why such collisions occur. Do such collisions occur as the result of limitations in the driver's rearward view or are there other factors? Are there some cases where the driver has a clear rearward view but chooses not to look? Why do the drivers make this choice? As an example, a Fault Tree Analysis can help to conduct an RCA for this situation as in figure 5.3.2.1 below.

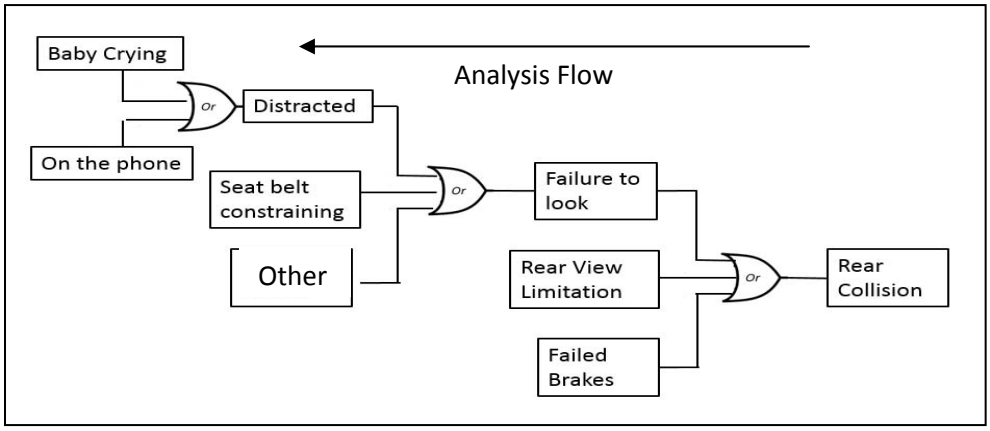


Figure 5.3.2.1 Fault Tree Analysis Example

Note that in this analysis, the "OR" gates present opportunities for errors to pass through to create a Hazard. Actually the analysis can go from the right to the left, starting from the Hazard (in a Hazard analysis) or the other way (for example in an FMEA). Also note that in some cases, creating the accident requires a cascade of events (e.g. baby crying ➔ distraction➔ collision) If however one provided a rear view camera, that would alleviate the Rear View Limitation issue, but one might still have a failure to look or failed brakes. Going a step further, one could provide a rear sensor with a beeping if the car gets in close proximity with an object in the rear, but this would only work if the driver paid attention to the sound – thus the introduction of this mitigation provides a new path for failure (driver not listening). On the other hand, if one added "AND" gates to the figure this might provide extra protection. For example, if one replaced Failed Brakes, with Brake Status Checked Okay Anded with Put In Reverse Gear one could prevent going in reverse if the brakes are not working. This is a change in the logic viewpoint and is a basic tenant of safety mitigation. This logic, however is fully depending upon the dependencies of the various causes.

Of course, if one could prevent a rear collision independent of any of the possible causes by invoking an energy field which stops all vehicles safely, then one might not have to worry about the specific underlying cause. (Well it doesn't have to be an energy field, unless proximity sensors count as an energy field, as shown in the commercials for Mercedes lately.) This energy field would be ANDED with all the other causes and would not allow flow to the Rear Collission Hazard. Therefore, in that situation one would not have to search back to root causes and leading to the important point that the level of the analysis depends in part upon the level of the mitigation that can be found.

5.3.3 Clinical Example

One can envision another, perhaps more complex example for which additional information is helpful. The table below represents that; and goes a step further in the indication of mitigations essentially incorporating a bit of a RCA into the table and adding a mitigation for the cause.

Table 5.3.3 Irradiation Hazard Analysis example

Hazard Description	Causes	Mitigations or Safety Decisions	Risk Cat	Sub system
Over-irradiation of the entire treatment field	1 The dosimetry system failed to read properly the dose	Provide a redundant dosimetry system, and/or further analyze the reasons in the FMEA.	3	A
	2 The Ion Chamber Electronics Unit fails to stop irradiation when the dose is reached	Provide a redundant dosimetry system, and/or further analyze the reasons in an FMEA.	3	A
	3 The accelerator fails to effectively interrupt the beam when instructed to do so.	Provide redundant beam shut offs and provide redundant signals to shut off the beam, and/or further analyze the reasons in an FMEA.	2	B
	4 An excessively high irradiation dose is requested by a human error,	Introduce strict dose entry procedures. Validate dose entry values, and/or further analyze the reasons in an FMEA.	2	C
	5. Treatment planning error gives the wrong dose	Introduce plan checks, conduct patient specific QA measurements, appropriate treatment planning system commissioning	2	C, D
	6 A patient is treated while the system is in dosimetry or tuning mode	Introduce strict system mode procedures. Provide redundant mode checking and/or further analyze the reasons in an FMEA.	3	C, D

Subsystems/Actors: A) Dosimetry, B) Accelerator, C) Therapist/Physicist, D) Software

In this table not only are the Hazard description and some causes identified, but a taste of mitigations are added (see section 7). In addition the Risk Category approach is used (arising from the RPN divided into categories) followed by a reference to the subsystem or actor which was considered in the input of causes. This table is meant to identify a thought process, not all the specific solutions.

5.4 Radiotherapy Radiation Hazard and Risk Examples

While the entire radiotherapy department workflow (section 8) should be considered in any safety analysis, one of the key factors of consideration is the resultant radiation Risk arising from any of the workflow steps. Therefore it is a particular topic of Risk to consider in more detail.

The following factors in the delivery of radiation are important:

1. The absolute dose
2. The relative distribution of a dose
3. The absolute position of the dose

From the point of view of radiation Hazards we essentially have two situations which can arise from any step of the clinical workflow:

1. Absolute Dose
    a. Overdose
    b. Under dose
2. Distribution
    a. One can argue that errors in the distribution are reflected in the errors of category 1 and 3 in any given location.
3. Position
    a. Inside the target
    b. Outside the target

One can consider the effects of this in the following table:

	Overdose	Under dose
Inside	Hazard Severity: Low	Hazard Severity: Medium
Outside	Hazard Severity: High	Hazard Severity: Low

If the dose outside the target is lower than expected then the normal tissue receives less dose and the Severity of the accident arising from this Hazard is low. If the dose inside the target is lower than expected, then there is a Risk of a failure to cure, which could be either a High or Medium Hazard, depending both on the treatment situation and on the subjectively on the individual doing the analysis. If the dose is too high, inside the target, then the main issue would be voiding a protocol, but there may or may not be a big Hazard. There may also be combinations of the above. Not everyone will agree with the assignments in this paragraph. Therein lies some subjectivity in the analysis and results of a Risk analysis.

Note, for example, that in particle therapy, an incorrect range (e.g. too deep) with a Spread Out Bragg Peak (SOBP) field can result in an overdose outside the target and a partial underdose in the target. In order to address the Hazards and FMEA appropriately, it is important for the analyzer to determine whether these all have the same Severity, or if they are different.

A lack of knowledge of the outcome should result in a worst-case analysis. For example, an incorrect contour could result in the incorrect dose applied, but if the treatment plan and delivery are correct the type of error could be determined. It may be likely that it wouldn't be caught early and therefore it would not be possible to know what treatment error resulted and the worst case assumption would

have to be used. Similarly errors in treatment planning algorithms, imaging simulations, and beam delivery will all result in one of the above. The situation would change however, if methods of detecting these types of issues were in place (e.g. in-vivo dose monitoring).

Thus one can see that there could be a certain amount of subjectivity to this analysis and one must carefully define the geometry and potential issues for their own situation. In the end, one must perform this analysis and as implied in the previous section

- identify the failures which can lead to this Hazard and consider the resulting accidents
- identify the Probability of the failure
- determine the overall Risk and from that the mitigation; e.g. frequency of the Quality check (See section 10)

Those safety items of highest concern are addressed with safety mitigations. Those issues of treatment precision may possibly be treated at a lower level of concern depending upon the tolerances identified. The remediation strategies are categorized as to their relevance to the various subsystems.

6. Failure Mode and Effects Analysis (FMEA)

The goal of a Failure Modes and Effects Analysis (FMEA) [14] is to identify failure modes which may result in Hazards and prioritize them for possible safety improvements. This method points in the BOTTOMS-UP direction. Whereas the Hazard analysis starts with a generic Hazard and asks the analyzer to imagine the types of causes, the FMEA examines, step-by-step, each action of the process, or component of the equipment and asks the analyzer to imagine what can fail in the step or how a component can fail and from that failure what effects, which may lead to Hazards, can arise.

6.1 FMEA Methodology

In its essence, the FMEA is simple. Briefly the following steps are to be performed:

1. Identify a failure mode from a component or a step (input)
2. Identify the effect of that failure (output)
3. Identify the Hazard that can result from this effect (this can be a multi-step analysis) (output)
4. Score the importance of that Hazard (output)
5. Create a mitigation (output)
6. Identify how that mitigation will be verified (Is a mitigation a real mitigation if you don't know whether or not it is working?) (output)
7. Optional – Rescore after each mitigation to determine if further mitigations are needed

The first step above is to identify a list of "failure modes" – things that can go wrong. In clinical radiation therapy operations this can be anything from a pure mechanical failure (e.g. wrong beam energy delivered) to a process-related planning error (e.g. wrong CT scan used for planning) to a mistake in clinical care (e.g. wrong delivered dose due to a miscommunication about prescription). This is in essence the same exercise advocated by Peter Pronovost and colleagues, which asks clinical staff to consider the question "How will the next patient be harmed?" [22]. Once the possible failure modes have identified, the FMEA formalism provides a method for ranking them in priority order. This

approach recognizes that time and resources are limited and that it is best to prioritize safety improvement interventions to target the biggest Hazards. Note that, what may seem to be a semi-random list of failure modes, can be better identified by noting the steps in the treatment workflow and realizing that there can be an error, as noted above in the appropriate steps.

What are the biggest Risks? FMEA provides a means to answer this by balancing various factors. For example, it may not make sense to prioritize a possible error that may occur only once in ten years even if that error might be fairly serious (the issue of Probability). A higher priority should be given to a failure that occurs once a month even if that failure has less serious consequences, especially if it is relatively easy to identify that failure before it impacts a patient's treatment (but this will depend upon the relative scoring of issues-see section 7). An interesting thought provoking question is, when is it necessary to install a traffic signal at an intersection? FMEA provides a semi-quantitative method to balance these factors.

When one sets out to conduct an FMEA, the first consideration, or input, is to identify which part of clinical care is going to be addressed. It is possible to analyze the entire workflow in radiation oncology from when the patient arrives for consult to their follow-up visit(s) [15], but the effort involved in this must be appreciated. It is often more productive to focus on smaller pieces, for example, the process of treatment planning. One can build upon this to assemble the entire workflow, however one must also take care that there may be interfaces among various pieces. For example if piece B and piece D are completed separately, it may be that piece B and piece D also depend/interact with piece A and each other. One of the inputs to this is the workflow or process map referred to in section 8.2. It is likely best to start with this for the entire process at a high level and then work out individual details. Another way to describe this has been mentioned earlier. Pieces that are simple enough to understand enable one to analyze safety more thoroughly. Pieces also interact with other pieces and these interfaces must be included in the analysis, but may possible just be another piece. Therefore, how one designs the system, or workflow can have a major impact on the complexity and effort involved in the analysis of safety. From the hardware point of view it is convenient to begin with a 'map' of the equipment and similar factors are considered.

Brainstorming sessions are often helpful to accomplish this analysis. Whatever the approach, it is crucial that representatives from all staff be included so that all aspect of the workflow steps and interactions among various disciplines are considered. A thorough understanding and appreciation of the subtleties of clinical care is essential, particularly clinical care in your department. A side benefit of this is the opportunity for getting various professional staff to communicate and understand each other's roles, and which beer they like. This, in and of itself is already a step for increasing awareness and fostering a culture of safety.

Once the list of failure modes has been developed some of the outputs include the identification of effects, and the Hazards arising from these effects. These Hazards are then scored in the same way as in a Hazard analysis. These Hazards arising from the failures become the link between the FMEA and the Hazard Analysis. Thus top down and bottom up meet and hopefully, fill in the gaps. As discussed earlier, various scoring scales have been proposed. The AAPM TG-100 report also has one. One should be careful to use what makes sense for the specific environment and not adopt an arbitrary scale, even one considered a standard if it doesn't make sense for your situation. The actual scale used is probably less important than the need for reproducibility in scores among staff using the FMEA tool for different activities, since after all these scores are only used to generate a relative ranking. The larger the range of the scores, the finer tuning one might do in determining action priorities.

6.2 FMEA Examples

The basic approach is the same when applied to either proton radiotherapy equipment or processes. An example of possible failure modes relevant to proton radiotherapy is presented in table 6.2.1 for certain steps of the processes that are part of proton therapy treatment planning. The examples here show various failure modes which result in an underdosed tumor due to inadequate plans. The Severity for all of the failure modes is listed as high (9 out of 10) since a target underdose has possible severe consequences to outcomes. Of course the exact consequences will depend on the clinical situation and the magnitude and location of the underdose, but here a worst-case scenario is considered. As in the automobile example, multiple failure modes can lead to the same Hazard. Note that if a Hazard analysis were being done, one might have identified treatment planning as a reason for an underdose (the Hazard), but the analysis may have stopped there with a mitigation such as 'double check the treatment plan'. Alternatively one could have gone deeper, but the benefit of the FMEA is that one starts at the bottom – or already deeper. The first failure is related to a process step which could be entitled "GTV delineation". The failure is an incorrect GTV delineation. This, in itself, could have several causes including a human error in reading the scan, drawing on the scan or the use of the wrong scan. Examples of wrong MRI scans might include an outdated scan from the patient or the wrong MRI sequence. While the effect may be independent of the cause of the failure and therefore the Severity of the Hazard is the same independent of cause, the particular cause may affect the Probability and detectability. In this example, it is scored as infrequent (P=2 of 10) but somewhat difficult to detect (D=5 out of 10) as it relies largely on the vigilance of the physician. Underdosing due to proton range uncertainties (#2 in table6.2.1) is scored as being somewhat more frequent (P=3) and difficult to detect (D=9) since there is most often no independent measure of the position of the distal edge of the Bragg peak in a patient without subsequent mitigation (such as patient specific QA). (Note that some developments such as PET scans, Prompt Gamma detectors and Proton Radiography are now beginning to address this concern and these may affect the detectability value.) The final cause of using pencil beam scanning inappropriately for a moving target occurs less often and should be easier to detect (D=7) since there would likely (if your department procedures include these steps !) be multiple independent reviews of the appropriateness of the technology for the case in question. Or, having these reviews could be an output of the FMEA as a mitigation to add to your processes. The RPN scores for these various failure modes now provide an indication as to which should be considered first for a safety improvement intervention. Here, it would be the issue of range uncertainty. Mitigations will be discussed further.

Table 6.2.1 Treatment Planning Partial FMEA

	Process Steps	**Failure Mode during Treatment Planning**	**Effects**	**Hazard**	***S***	***P***	***D***	***RPN***
1	GTV delineation – load the MRI Scan	Wrong MRI scan loaded	Incorrect GTV delineation	Tumor underdosed	9	2	5	90
2	Application of Tx Plan margins	Incorrect Range uncertainty used	Incorrect Plan	Tumor underdosed	9	3	9	243
3	Determine if motion mitigation is needed	Choice to not use 4D CT	Fail to include target Motion and wrong volume targeted	Pencil beam scanning applied inappropriately to moving target Tumor	9	1	7	63

Table 6.2.1: Example failure modes and Risk scores for proton radiotherapy treatment planning. Scores for Severity, S, Probability of occurrence, P, and detectability, D, which are multiplied to compute a Risk priority number, RPN=S×P×D.

Table 6.2.1 highlights some issues that are worth further discussion. First, failure modes are dependent on the processes and equipment in place. Failure mode #3, for example, related to pencil beam scanning may not be relevant to facilities that only treat such patients with uniform scattering systems, although even in that situation the use of gating and adjusted treatment volumes are sometimes warranted. Processes are clinic dependent as well. A clinic that already has mitigations, such as peer-review, in place for treatment related imaging [23], for example, would likely have a better detectability score for this failure mode. Note that this reflects a sometimes iterative process. High Risk results in a mitigation output which, when reanalyzed results in a lower Risk. This is sometimes done until an acceptable (subjective definition perhaps) level of Risk is reached. All of which underscores the fact that FMEA must be performed by each clinic, and though example failure modes may be derived by sharing information between clinics, the details of FMEA scoring need to be consistent. A final feature to note in table 6.2.1 is that some failure modes will apply equally well to proton as to photon radiotherapy (example #1). This highlights the value of possibly sharing information between practices, a concept that will be discussed in more detail below.

Shifting now to an example of an equipment failure, helps to give insight into other aspects of FMEA work. One may consider a beam delivery subsystem in which there is an ionization chamber, which requires a high voltage power supply. Consider this power supply to be a component. One can, of course, go further and consider a particular resistor in that power supply as a component, however, through an understanding of the system functionality, one can identify various failure modes of the power supply without having to look at the failures of each resistor and capacitor. In more complex systems further analysis may be necessary. In the case of a power supply, one can consider a simple finite number of failures such as wrong voltage or current. In fact, what is being done in this instance is to identify a cut-off for the analysis based partially on maintenance and spare parts considerations. One is unlikely to decide to implement safety mitigations at the resistor level, but rather detect the error at the output voltage level. That is not to say that the power supply manufacturer might elect to design the power supply with sufficient redundancy so as not to cause a problem if one particular resistor goes bad, or to monitor the value of that circuit.

One example of a wrong output voltage is that it goes to zero. The following thought process can then be followed:

- Component: High Voltage on an Ionization Chamber
- Failure Mode: High Voltage turns off
- Effect: MUs will not be counted
- Hazard: Overdose
- Severity: High
- Probability: Medium
- Detectability: High (if one implements methods for this detection)
- Result: Mitigation required for detectability

It may be instructive to examine some more detail as to the process thought that can go into this situation. In this report, the section on mitigation is separate from the sections on Hazard analysis and FMEA, however in practice they should be dealt with simultaneously. The following diagram in figure 6.2.1 is an example of possible considerations resulting from this seemingly simple failure. Among the considerations embedded in this diagrammatic thought tree are the following:

- Can the failure be detected by hardware?
- Can the failure be detected by software?

- What types of redundancy can be implemented to identify that the failure has occurred (e.g. a second ionization chamber)
- What if the detection doesn't work?
- What failure modes are possible if the SW detection method is employed?
- What are the actions to take if this situation is detected?
- What detection is necessary to ensure that the desired action(s) take place?
- What further action is needed if the desired action(s) do not take place?

Okay, you won't find a "thought diagram" in the literature. This type of consideration is most compatible with an "Event Tree" (figure 6.2.2). It is not a fault tree because it doesn't start with a Hazard, and it not an FMEA because it doesn't factor in the consequence of the failure. It looks at an error and follows the path of the mitigations, catching the error and reacting to it. This thought diagram is an example of analyzing the situation the way one thinks about the problem. It's not always the case that a particular analysis can be made to fit into a standard format. For example, the event tree from this diagram in figure 6.2.2 does not include the 'diagnostics' boxes in figure 6.2.1 (e.g. network failed) which could lead to more detailed branches of why a software error would occur. But the event tree would force these to be sequential rather than potentially parallel. However, it is sometimes the case that a more standard format will help the analysis become clearer and complete. (e.g. the event tree includes some Probability estimate.) This is a very important consideration when deciding upon the tools for the analysis. Exactly how far one goes in this analysis depends in large part on the Risk and on the system complexity.

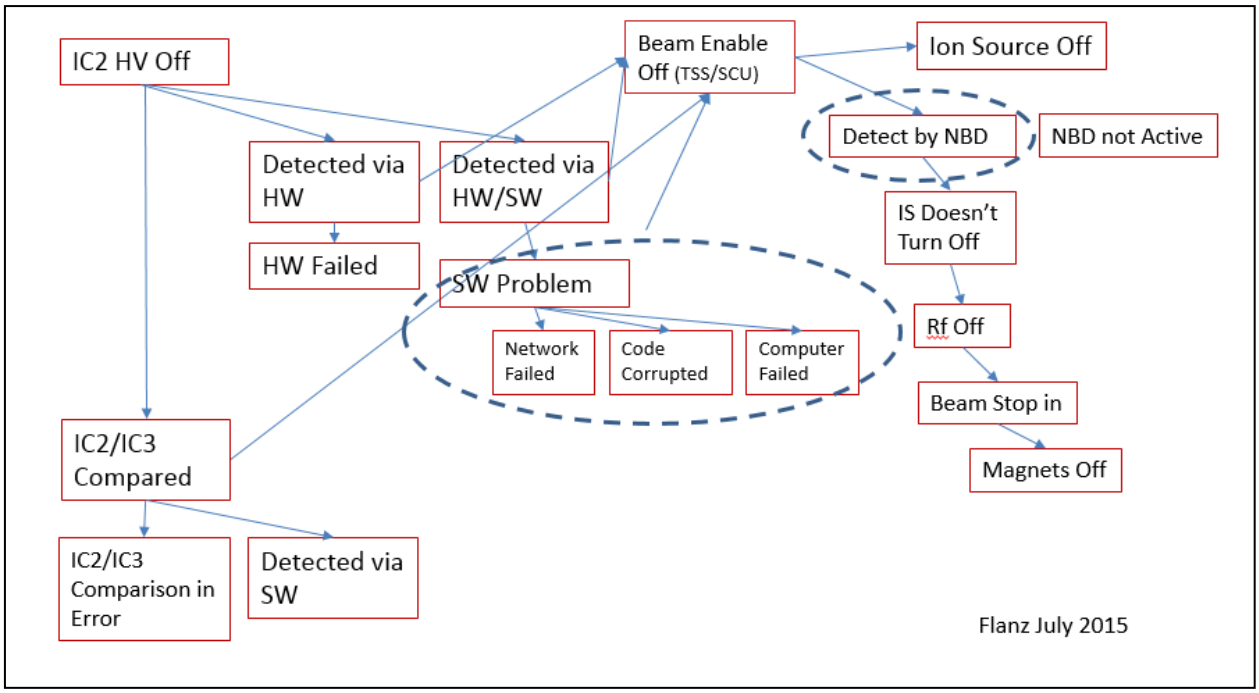


Figure 6.2.1 Thought diagram following the threads for a fault and mitigation

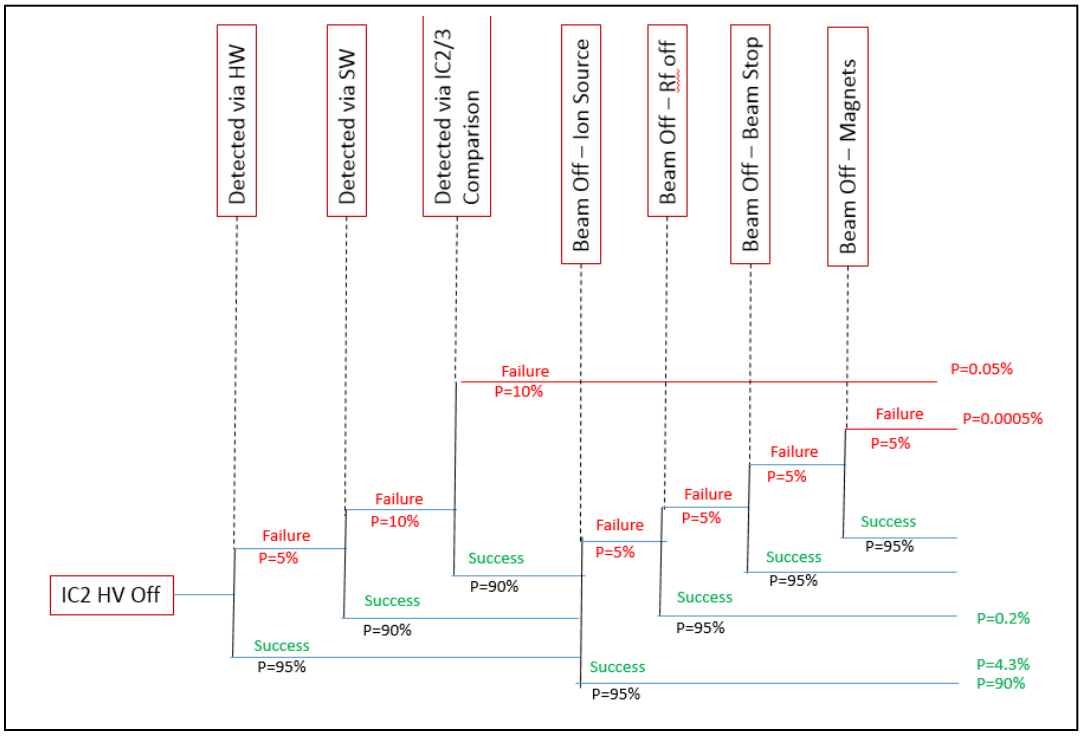


Figure 6.2.2 Conversion of Thought diagram into an Event Tree

6.3 Tools to help formulate an FMEA

Recognizing that the tables offered are not a replacement for the thought analysis and interdisciplinary discussion, one can sometimes use the tables as an aid in the thought process. The following table headings represent an evolution over a number of years of working with equipment for particle therapy systems. The first image below table 6.3.1a) is actually the left side of the table and the second image below (table 6.3.1b) is the right side of one full table. It is helpful to see that this table goes in the direction of the considerations of the above 'thought tree'. At the left it presents the opportunity to drill down to the desired component level and identifies the failure mode and the effect. This effect is further deconstructed to specific issues related to beam properties and in turn specific issues associated with treatment Hazards. Up to this point, the system/subsystem columns can be replaced with steps/sub steps of a process and the beam property columns can be eliminated for non-beam-generating-equipment. (Note that effects on the equipment – e.g. damage to the equipment – is included. If the equipment is damaged, that results in lost treatment, which in itself is a Hazard.) Next the RPN analysis is accomplished with mitigation considerations (see section 7). The RPN results in a level of Criticality and a column exists for the level of redundancy required based upon that Criticality. Finally, in addition to mitigations spelled out, the desired irradiation state that the system should be in, if that failure occurs is identified, as well as the conditions of critical elements of the system to ensure that the system state is appropriately safe. Note that there are several approaches from here. One can use the level of Criticality to determine the mitigation levels needed, or one can iterate, as noted earlier and keep recalculating the RPN after the introduction of each mitigation. Such strategies need to be addressed upfront. Note also that this table does not call out detectability or avoidability explicitly, it is assumed to be in the Probability.

Table 6.3.1a FMEA Example Table part A

					Effect on Beam Properties			**Treatment Radiation Hazard**		**Mechanical Hazard**	**Equipment Hazard**			**RPN Analysis**			
System	SubSystem	SubSubSystem	Failure Mode	Failure Effect							No danger to Patient			Probability	Severity	Category (RPN)	Redundancy Level
					Position	Size	Range	Target Dose	Outside Target								
	Scan Mags	Power Supply	No Volt	Worng Pos	x			x	x								

Table 6.3.1b FMEA Example Table part B

Mitigation A1	**Mitigation A2**	**Mitigation B1**	**Mitigation B2**	**Mitigation B3**	**Even More Mitigations**	**Mitigation F1 (multi)**	**Mitigation S1 (multi)**		**Irradiation State**				**Machine State**					
Equipment Prevention	Protocol (HUMAN)	Hardware Detection	Hardware Detection	Hardware Detection	??	Functional Detections	Software		Nominal End	Pause	Abort		Injector On/Off	Accelerator Rf On/Off	Beam Stops In/Out	Beamline Magnets	Scanning Magnets	

A couple of examples of this approach are shown in table 6.3.2.

Table 6.3.2 Example Equipment FMEA Table

ID#	Process Step or System Component	Failure Mode	Failure Effect	Hazard	Probability	Severity	Category	Mitigation 1 Protocol	Mitigation 2 Protocol	Mitigation 3 Hardware Detection 1	Mitigation 4 Hardware Detection 2	Action
1	Deliver Beam/ Ionization Chamber	IC Voltage is wrong	Wrong dose is read	Possible Under or Over Dose	2	4	IV	Perform QA	??	Provide HV Readout	Provide Redundant IC	Pause Beam when Detected
2	Load patient prescription	Wrong Patient is in the room	Wrong patient/Wrong Rx is treated	Wrong dose delivered to patient	2	4	IV	Confirm Patient ID Verify Patient Rx (Time-out)	At least 2 people perform these checks	Provide ID Scan method		

6.4 FMEA Limitations

Having understood the basics of FMEA it may be useful to briefly discuss some of the limitations. The first is practical and has to do with effort and usability. FMEA is sometimes thought to be so labor-intensive as to be almost unusable. This is largely a myth which is the outgrowth of early experience. The FMEA exercise of Ford et al. [15] required five months of weekly meetings with an 11-member steering committee. That study considered the entire radiation oncology workflow, which is very ambitious, and was conducted at a time (2007) when FMEA was essentially unknown in radiation oncology. The learning curve is considerably less steep now. A more recent study by the same group demonstrated that FMEA for the full radiation oncology process could be conducted in four one-hour sessions and showed a measureable Risk reduction. A number of other studies have appeared in the radiation oncology literature demonstrating the usability of FMEA. The view of FMEA as a difficult tool may have also been promoted by the fact that AAPM Task Group 100 on FMEA has been over ten years in the making and, when complete, will likely be one of the longest Task Group reports published. It must be appreciated, though, that a substantial effort of this committee to develop a comprehensive report does not necessarily translate into a tool that is difficult to use. With the right understanding, preparation and guidance FMEA has been found to be usable. At least some of the authors also believe that the lack of understanding of the difference between a Hazard analysis and an FMEA can add complexity to the process. The Hazard analysis is a real help in getting one's mind into the process and the FMEA then follows up with details.

Other limitations of FMEA are more fundamental in nature. The first, and most obvious, has to do with the scoring system. S, P and D scores are subjective and highly variable between people. This translates into an uncertainty in RPN-based ranking of failure modes. As such it is not very meaningful to spend any substantial effort examining FMEA rankings in fine detail and certain can be problematic if compared among institutions. The rankings are best suited for identifying the most obvious Risk points, the outliers in terms of RPN. At an even more fundamental level, the concept of prioritizing Risks by a simple multiplicative product of S, P and D is probably over simplistic. This approach has never been independently validated to our knowledge, and many questions remain. What is the particular significance of the multiplicative product of S, P and D? Why shouldn't Risks be prioritized by some non-linear combination of these variables for example? In healthcare the Severity, S, should perhaps have a particular importance over the other three factors. As yet, there are no satisfying answers to these questions. Still these would affect the thresholds for action perhaps, while the absolute numbers may not really be relevant.

In spite of the many limitations of FMEA it is still a useful tool when employed right. FMEA, together with the Hazard analysis are a couple of the few prospective methods to reduce Risk. It is also relatively easy to use, and is at least effective at identifying the highest possible Risk scenarios. It is recommended now by TJC, ICRU and the AAPM with other organizations likely to follow. Finally, the specific Risk mitigation aside, the FMEA tool can provide a rally point around which different professional groups in a department can communicate about patient safety and the quality of care. The level of detail in Hazards and causes is a common pitfall of the techniques. This is one of the reasons why it is so helpful to have a top-down (hazard analysis) AND bottom-up (FMEA) approach to bridge the detail gap. The more specific the information provided the better. It must be recognized that detailed information comes at the cost of complexity and effort. In many cases, for radiotherapy workflow the level of detail does not have to be high, but as one delves into the details of machine operation, the reverse is usually the case.

7. Mitigation of Risk

One of the outputs of the various analyses discussed above involves the mitigation of potential Risks. The Risk potential numbers (RPN) have been estimated and calculated and what remains is to identify how to reduce the importance of any given Risk. Although, mitigation is arguably at least as important as the identification of Risk, relatively little literature is dedicated to it. This is certainly true in the radiation oncology literature, but is also apparent in the patient safety literature as a whole. The safety improvement mitigations that have had some measureable impact, like the use of checklists to reduce central line-acquired bloodstream infections, have generated a great deal of notice and excitement [24].

7.1 Mitigation Strategies

It remains now to determine how to practically address issues that arise in the various categories. One method is to introduce a mitigation for a particular failure or Hazard, determine in some possibly subjective manner the degree to which this mitigation reduced the Probability or Severity of the Hazard, and continue to introduce mitigations until the Hazard category is reduced to an acceptable level. While it is easy to see how a mitigation may reduce the Probability (e.g. through detectability or avoidability), it is more difficult to understand how it may affect the Severity, unless it was somehow fundamentally changing the actual Hazard or changing the way that the Hazard propagates into an accident. The Severity score for "car will not start" (in section 5.3.1) is low since this is not thought to affect safety. One might, however, consider a situation in which the car is going to be used to bring someone to a hospital. Would the Severity in such a situation change?

Another method is to define a high level strategy of mitigation based upon the category of the Hazard. For example, a category IV (4) (e.g. section 3.2.1) Risk may invoke the introduction of redundant sensors or a second look by another individual, or the imposition of a non-software means of mitigation, or redundant mechanical supports, whereas a lower category Risk may allow for software mitigation methods or human check alone. Different types of mitigation may either reduce the frequency of a Risk (e.g. by avoiding it completely) or minimize the Severity of a Risk (e.g. by an interlock stopping the irradiation faster than otherwise possible).

Below is an example of potential Hazard from a Hazard analysis (not an FMEA) associated with "Ionizing Radiation" and the potential mitigation methods that are considered to be applied in that case. In this case only protocol methods are implemented, as opposed to additional sensors or interlocks. Is that enough?

Table 7.1.1 Ionizing Radiation Hazard Example

#	Hazard	Cause	Subsystems		Risk				Mitigation Measures	Verification Method
			Imaging	Beam Delivery	Severity	Probability	Avoidance	Risk		
1	Unnecessary Exposure	Respiration Gating interface during imaging failure	Y	N	4	3	1	12/ I	1) Watch the Respiration signal on a monitor. (Protocol) 2) Perform regular QA with moving phantom. (Protocol) 3) Perform imaging with and without the gating system (Protocol)	Test Plan to verify mitigation is working…

7.2 Mitigation Types

Grout [25] identifies three ways to address Risk.

1. Make the Risk impossible (e.g. provide a round hole so only a round peg can fit into it)
2. Make the error visible. (Provide the appropriate instruments and display)
3. Create a fail-safe design (Self detection and/or self-reacting – e.g. Normally open relays)

In the language that has been used throughout this report, it would be important to reduce the Severity and Probability, the latter sometimes by improving the detectability of the issue which could give rise to a Hazard. A practical question is whether it is possible to address all the Risks that will be identified and indeed whether all the Risks are necessary to mitigate. However, these three approaches do not tell the whole story regarding how mitigation is applied to radiotherapy beam delivery and this will be discussed in the following sections. If we first concentrate on these three approaches we note the following. Preventing errors (#1) corresponds to reducing the Probability of occurrence, *P*, of a failure mode. Making them more visible (#2) relates to, *D*, detectability, and fail-safe design (#3) reduces the Probability of a particular even happening to zero (assuming that the Probability of the fail safe design being fail safe is 100%).

The first mitigation listed above is often advocated as the strongest error-proofing approach, and corresponds to the ”affordances” in the design work of Donald Norman, i.e. a feature or design that does not allow a device to be used in the incorrect way [26]. It is sometimes possible for clinical users to employ forcing functions through software or process design, but more often than not such “bullet proof” design is not feasible for a clinical user. Furthermore, in several aspects of radiotherapy, particularly beam delivery, this method is simply not possible. The delivery of the prescribed dose is predicated upon a measurement, with its inherent error. It is not possible to prevent the delivery of a dose higher or lower than prescribed, but it is possible to detect that the dose that is desired is close to being reached, or has just been exceeded and to then react quickly enough, or with enough foresight to initiate the process of turning off the beam which will happen in time to ensure that the beam delivered is within the desired tolerance. This is not the same as preventing the incorrect dose from being delivered as opposed to reacting fast enough once the dose gets close. Perhaps this is closer to the second strategy.

The second mitigation strategy listed above of making an error more visible is very commonly employed in the clinic. The structure of quality assurance in radiation oncology may be viewed as essentially a way to make errors more visible. This may be done, for example, by measurement of a beam prior to its delivery in patients or by independent checks of a treatment plan by a medical physicist and a radiation therapist. Such quality assurance measures are advocated in AAPM Task Group-40 from 1994 [27] and many other society recommendations. Recent work has attempted to address which of these various quality control checks is most effective [28]. This study reveals interesting patterns, such as a strong effectiveness of physics chart checks and a weak effectiveness of pretreatment plan measurements, but more work remains to be done.

The categorization of mitigation strategies listed above is not all-inclusive, and some recurring themes are not mentioned, for example, the need to provide continuing training and education to staff or the need to establish staffing levels that are appropriate to the clinical workload. Issues like these do not fit neatly into the Grout et al. design schema, but their utility in mitigating errors is clear. The more general

issue of establishing a proactive Quality Management program includes many elements of raising a culture of safety and internal review which can lead towards effective mitigation strategies.

In the following sections we further break down the mitigation strategies.

- Mitigations through Protocol and Communication: This is a category which attempts to prevent a Hazard through human based information and procedures.
- Mitigations through Quality Assurance: This is a category which attempts to visualize system problems through regular measurements. These measurements occur at various time intervals. The reaction to a finding must be determined and implemented in design and/or protocol.
- Mitigation through Equipment Safety Design: This is a category which attempts to either prevent, or if that is not possible, to minimize the Hazard by specific design implementation, or measurement capability together with methods to end the source of the Hazard.

7.2.2 Mitigations through Protocol and Communication

The most influence that the facility staff has on ensuring a safe process is the influence on the internal facility processes and the roles that the personnel involved in these processes are assigned. A better understanding of the possible errors that can results without appropriate process mitigations may help to motivate staff to participate in these mitigations which can lead to reduced numbers and Severity of errors.

7.2.2.1 Training

The International Atomic Energy Agency (IAEA) has a long tradition in collecting information about radiation accidents and analyzing the backgrounds. In a safety report on accidental exposures in radiotherapy [29] it was demonstrated that one of the most frequent source of accidents is connected to the personnel in an institution, namely a lack of education and a lack of communication. Education and training of personnel

Education here is mainly related to training to work with a dedicated system and it includes proper training by the institutions and as well as by the vendor. The institution has to take care, that all members of a team receive training in different areas:

- Regular training in internal regulations: these include typically all safety regulations in a facility, as well as radiation protection regulations and regulations about data privacy etc. and include also all existing Standard Operating Procedures (SOP).

- Regular training on the dedicated systems used for radiotherapy: this may include the vendor but often is done by the institution directly through a train-the-trainer approach. It includes basic instructions how to work with new system, but also information about changes or updates of a system. Also the users should be informed about the intended use of the products.

- General continuing training on the job: this includes all kind of teaching activities like teaching courses on different subjects, regular seminars or advanced courses for specialization.

Proper training on a system usually requires not just theoretical but also hands-on training at the system, which needed additional resources. Another important prerequisite is appropriate documentation material, which may again be provided not solely by the vendor, but in parts also by the institution (if special procedures are to be followed). It may be important to note that all relevant

documentation should be available in the native language of the user institution (requiring sometimes multiple versions of a document).

The training on internal regulations plays a special role, as it includes all regulations which have been implemented, in order to mitigate certain Risks in a facility. Here is the place where additional regulations have to be included if a Risk analysis team comes to some new conclusions. Documentation of the participation of the personnel is therefore required as a proof that the mitigation measures have been realized successfully.

7.2.2.2 Communication about safety-related issues in an institution

Another factor of high priority should be the communication structures in an institution. It is important for the personnel to know the safety and quality philosophy of an institution, the background of certain procedures, Standard Operating Procedures (SOPs) or regulations and to be informed about the actual status of the system and the activities around it. Proper communication structures also have to insure a proper flow of information, so that all relevant information reaches the personnel in charge. A robust safety culture facilitates routine reporting of possible Hazards and other issues which eases the desired communication flow. To illustrate this some examples are given here.

The vendor of a system may be informed by an accident in another institution and come to the conclusion that a product warning has to be issued. This is a regulation by the vendor, to be followed by all users of this system in order to mitigate the Risk of repeating this mistake. Such a product warning is typically sent to a single contact person in an institution (e.g. the head of Medical Physics, or to a regulatory person). This contact person has to ensure proper distribution of this information to all involved groups in an institution and may also start an internal discussion, if changes in the clinical workflow or additions to the internal regulations have to be made.

Another example is the software update of the vendor of a treatment planning system, which has just been installed on the TP computers. This update may include a bug fix and result in changes of the dose distribution in some special situations. In this case it is important to inform not just the Medical Physics team about the potential improvements, but also the radiation oncologists, to make sure they are aware of these changes and they can accept them. In may also be necessary to demonstrate the changes and discuss the possible effects on dose distributions in a dedicated training session.

- In order to secure the proper flow of information, it is useful to have dedicated regular meetings for various groups, involved in different tasks, where the relevant information is distributed: General Medical Physics meeting
- Treatment planning meeting involving physics and medical personnel
- Clinical meeting involving medical and medical physics personnel
- Technical meeting involving accelerator personnel, technicians and physicists
- Team meetings involving all groups in a facility

7.2.3 Mitigation through Quality Assurance

Not every aspect of the beam specification and delivery process is possible to verify before or during the treatment process. A clear strategy to define the types of measurements to be defined with the appropriate frequency is absolutely essential. One possibility is to follow the QA steps identified by consensus reports such as AAPM TG 142, however, even such reports indicate that every radiotherapy

facility is a little different and the staff must identify the appropriate procedures to follow for their facility. Section 9 discusses this in more detail.

In the case of particle radiotherapy there are primarily two modes of beam delivery. One is beam scanning and the other is beam scattering. There are certain beam parameters that are important in each case and they will affect the QA measurements and frequency of the measurement.

7.2.4 Mitigation through Equipment Design

It should not be expected that all staff in a facility should understand all of the detailed safety mitigations in a radiotherapy system. It is a goal of this report to provide some background to enable the reader to ask questions if desired.

In the car example, failure modes would also presumably depend on the type of automobile under consideration. The occurrence score for an electrical short in Jaguar for example will be very high while for a Volkswagon it will be very low. Similarly the occurrence for "Collision – Back up into something" may be lower for a sedan but very high for a mini-van with more limited rear visibility. One may need to have a separate table entry for each make and model of car. Similarly the analysis will be different for each radiotherapy department and type of equipment.

Basically there are two basic tasks that are relevant. A device in the equipment is set and the value to which that device is set must be measured with a specified accuracy. Depending upon the level of potential Risk of incorrectly setting this device, there may be additional redundant ways to measure the setting of this device. In addition, one can also require a "Functional Redundancy", or a redundant measurement to ensure that the function desired has been performed. For example, if the function is to deliver the appropriate, accurate dose, a dosimetry monitor chamber would be required. One could, for example, argue that if one knows the beam energy and the charge delivered from the accelerator into the patient, or the settings that have been applied, that this is sufficient information. One can in fact argue that point, however the standards required redundant monitor chambers as shown in figure 7.2.4.1 below.

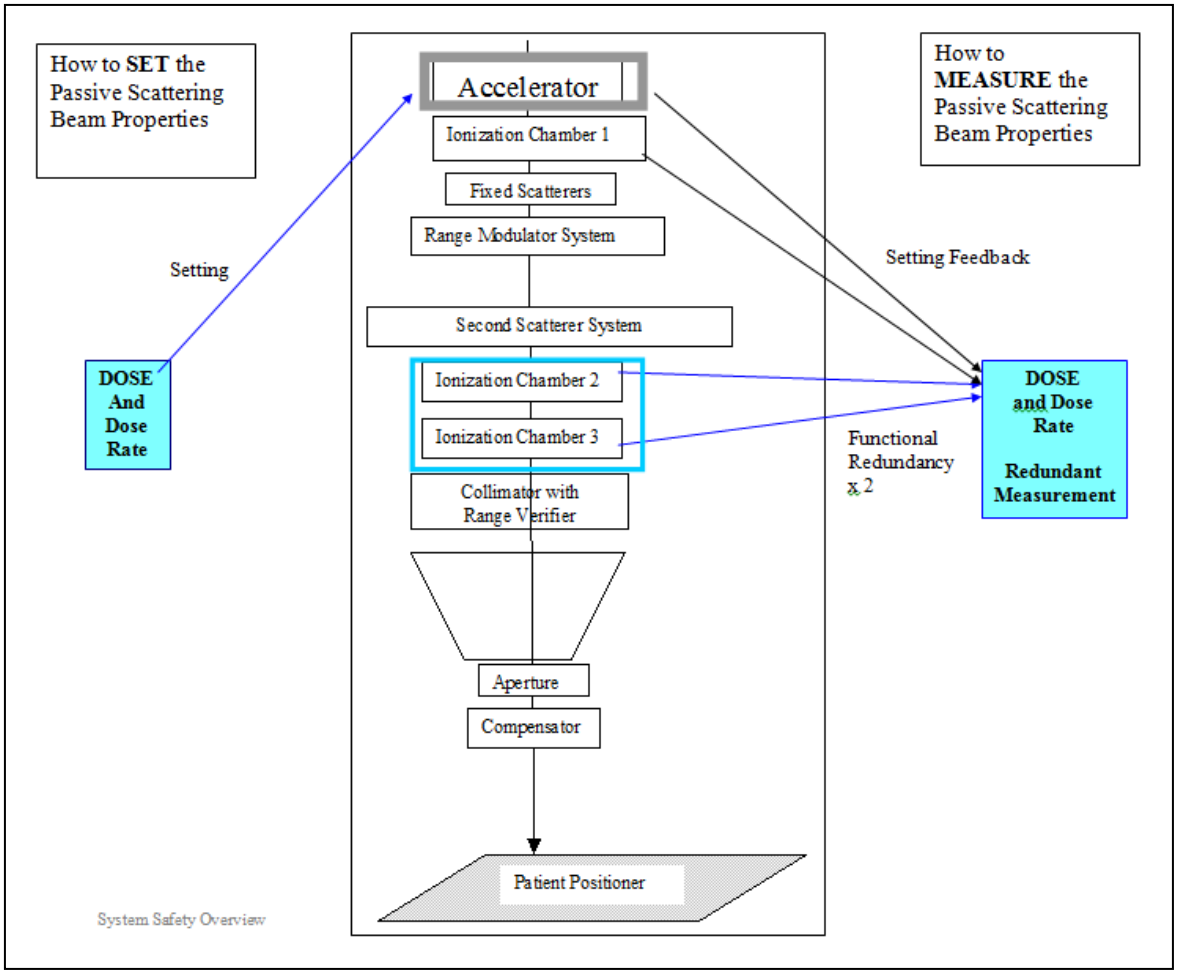


Figure 7.2.4.1. Example of how settings and functions are both redundantly monitored

7.2.5 Standard operating procedures

A considerable uncertainty in all procedures involved in the radiotherapy process is the above mentioned human factor. All humans err and consequently they may introduce Risks at any stage of the treatment process. However it is not necessarily appropriate to offload all responsibility to a machine (a Risk analysis would have to be done). One way to limit this human Risk is to define standard operating procedures (SOPs) for the most important processes. These may include SOPs for QA and Quality Control (QC) procedures but also parts of the clinical workflow. One example of a very critical QC procedure is the daily monitor calibration, since it directly affects the dose applied to all patients at that day. It usually involves the setup of a phantom, a dose measurement and some kind of analysis. The correct performance of any of these steps requires some kind of expert knowledge and there are numerous ways to introduce errors, many of them too small to be directly visible. Problems arise typically, when a new persons joins the team.

In order to make every detail of the measurement very clear without ambiguity, an SOP is very useful. Such an SOP should always be considered a working document, i.e. it is necessary to collect the feedback of the team working with the SOP and add new aspects or comments to continually improve

the SOP. An excellent source for improvements of SOPs, are the comments from new people being trained on the system.

It may, however, be daunting to think about writing SOPs, but as soon as they exist, their value becomes immediately clear:

- it makes the procedure more straightforward to do (less error occur);
- it may allow involving more people from a team into procedures, that were hitherto thought to be an expert's matter (better use of resources);
- it's invaluable to all new members of a team (shorter learning curve);
- It's important in a Risk analysis to have a clear description of a process.

A good example for the SOP for a clinical procedure is the patient set-up, as it is crucial to the whole treatment and may be a relatively complicated procedure when image guidance is used (which is the case in the majority of particle therapy centers). The X-ray imaging systems, patient positioners, matching algorithms and position correction strategies offer numerous possibilities to allow for many small deviations in the achieved accuracy. Here, the aim of an SOP is not so much to provide the best way to set-up the patient, but to provide a standard way, which is comparable for all patients. Only when a standard is defined, one can start analyzing different procedures and try to improve the process. It should also be noted that SOPs are often the result of a Risk analysis, trying to mitigate Risks arising from unclear and vaguely defined, but critical processes.

It is important, however, not to exaggerate the use of SOPs and other regulations, and limit them to procedures where there is consensus about their usefulness. Otherwise people in a team may feel like not carrying any responsibility for their work any longer and not having to think about the process they are performing. This would be in any case counterproductive.

7.3 Example Mitigation Implementation: Highway Safety

With this background, we now turn our attention to an example to appreciate how error mitigation might develop in practice. We consider the example of automobile safety discussed in Section 5 (Table 5.3.1). Though this is somewhat artificial it illustrates the important points.

As an official of the National Highway Traffic Safety Administration in the early 1970s you have completed a comprehensive assessment of automobile safety using FMEA. The results (Table 5.3.1) indicate that some of the highest Risk failure modes are collision due to backing up (*RPN*=125) and collision due to speeding on a dark road (*RPN*=50), and you decide to address these with mitigation strategies.

First let's consider what won't work. You could conduct a public relations campaign to remind people to take it slow on roads, obey the speed limit, and watch out when they are backing up. You could send out fliers and place ads and so forth to raise awareness. You might as well save your breath, however. You would be going against decades of accident investigation that has shown that reminders and the like are almost entirely ineffectual. The idea of sending out reminders may seem reasonable, and it is a very common error mitigation invoked in clinical practice, despite its ineffectiveness.

Upon more careful reflection of the mitigation principles discussed above you might attempt principle #2 instead, and make an unsafe situation more visible to the people involved. You might try to reduce the speed of automobiles on highways by redesigning the speedometer. A meter that has a maximum speed of 85 miles per hour would more obviously alert the driver to their speed. At 55 miles per hour the dial would already be well past half its range. (In fact this is just what the National Highway Traffic Safety Administration did in 1979 until the requirement was eliminated in 1981 due to strong consumer resistance!).

As a second approach you might try building in a fail-safe (or safety-by-design). That is, try limits the injuries if a collision does occur. This is the third principle listed above. You might require the availability of seatbelts in cars as was done in 1968, but then you would quickly realize that many people do not wear seatbelts. Rather than launch another failed public relations campaign, you might consider requiring the availability of airbags. (This is what the NHTSA did in 1994 for the driver's side and then in 1998 for the passenger's side). This strategy of safety-by-design is also the basis for the growing number of assistance systems in cars, like e.g. automatic reduction of speed when getting too close to other cars. An ultimate implementation may be in self-driving cars, which is getting closer and closer to market. While this may take the burden of back-up collisions off of the human driver, is it safer? If it is safer, perhaps it's because of the safeguards that are necessitated by the self-driving nature of the car, and would those same devices have helped the human driver?

In reality, as discussed above, you would need to conduct a much more detailed analysis to make any progress on this issue. You would need to understand why collisions are happening on dark roads: which roads, and under which conditions, etc. Say that an important issue turns out to be drivers colliding with parked cars on certain stretches of road. You might install more streetlights (make the Hazard more obvious) or install speed bumps (make the driver's speed more obvious to them). In the case of collisions in backing up, you might install proximity sensors or rearview cameras on the vehicles that are most at Risk such as mini-vans. The details quickly become important, but as in healthcare, the details are crucial to developing an effective mitigation strategy.

8. Patient Treatment Workflow

Safety is a mindset that must be practiced throughout the patient treatment experience. It is not only how the machine performs, but how a myriad of personnel and systems perform. Radiotherapy is a unique multidisciplinary collection of activities which must be included in any evaluation of Risk and mitigation to help ensure a safe experience. Before one should perform any sort of formal analysis, it is important to put that analysis in the proper context. One must identify the processes involved in the treatment of a patient, and not limit oneself to only the mechanical and software issues associated with a given radiotherapy machine. This already provides a strong constraint in the analysis. It is assumed that those performing the analysis know the field and know how to perform such analyses (these could be different groups of individuals). These processes include the activities performed before using the radiotherapy equipment and include other equipment used, whether interfaced or not, to the radiotherapy machine. John's Hopkins has applied FMEA methodology to the enhancement of the safety of their process. Here is an excerpt from http://www.hopkinsmedicine.org/news/publications/quality_update/winter_2011/looking_forward_to_adverse_events . *"Our process is extremely complex, containing nearly 300 steps between the time that the patient arrives for consultation to treatment. Between those points there are multiple sub-processes, such as simulating treatment or contouring tumors. If you sit and wait for an error to occur at*

just any one of the hundreds of steps, and then try to prevent that same error from recurring, it's unrealistic to expect that you'll be effective. The next error will likely occur at a different step or in a different way. We turned to failure mode and effect analysis to help us to systematically look at these potential errors."

While it is not the purpose of this report to provide a definitive workflow, it is thought that identifying the considerations within various aspects of clinical workflow could lead to a possible workflow scenario which the reader can modify and begin to develop information about her/his process.

There are at least five main steps in the treatment process [15]. These include:

1. Consultation
2. Simulation
3. Treatment Planning
4. Physics Quality Assurance
5. Patient Treatment
    a. Personnel Actions
    b. Machine Actions

Sometimes this process is considered differently. For example steps 2 and 3 may be combined into one step that includes imaging, planning and simulation. Also, one might consider adding follow-up as an additional final step. In any case, the entire process, or each of the steps of the process can be visualized as a map. This map could be a list of steps organized in nominal order of time, or even a flow chart, including decision points and control flow.

The delivery processes for particle therapy are complex and are a rich environment for potential errors. Like most of heath care, particle therapy may be life-saving but is also potentially dangerous when errors are made. The Institute of Medicine, in '*To Err is Human*' [30] has asked the medical community to provide each patient with the highest quality care at each single encounter. High reliability organizations (HRO) in health care are those that have created environments with reduced system failure and have effective responses when failures do occur [31]. A significant component of the success of HROs is a strong safety culture. The relationship between a strong safety culture and high reliability is well known [32] and can be measured with a widely available tool from the Agency for Healthcare Research and Quality (AHRQ) Patient Safety Culture Survey [33]. The AHRQ surveys 12 organizational attributes:

1. Communication openness,
2. Feedback and communication about error,
3. Frequency of events reported,
4. Handoffs and transitions,
5. Management support for patient safety,
6. Nonpunitive response to error,
7. Organizational learning-continuous improvement,
8. Overall perceptions of patient safety,
9. Staffing,
10. Supervisor/manager expectations and actions promoting safety,
11. Teamwork across units, and

12. Teamwork within units.

These attributes provide a useful framework to help organizations begin the difficult work of maintaining a robust safety culture.

8.1 Consultation

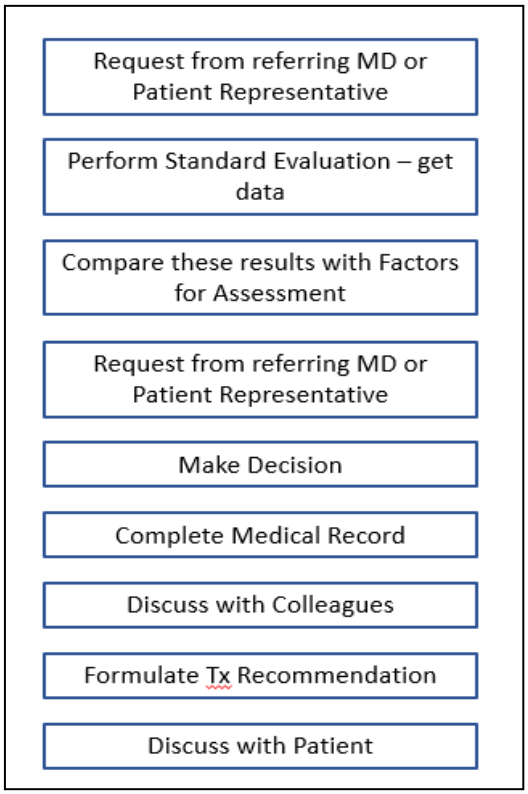
The consultation process for particle therapy is and should be similar to that for general photon radiation oncology as well as other medical specialties. A consultation generally begins with a request from a referring physician or a patient/patient representative to evaluate for the appropriateness and medical necessity of delivery of particle therapy. A physician will typically perform a standard evaluation with history-taking, physical examination, and review of objective data such as pathology reports and imaging studies. Prior to making a decision about the medical necessity and appropriateness of particle therapy, a physician may order additional tests.

There have been several attempts [34] to define those factors which must be assessed as part of the decision-making for radiation therapy and a comprehensive list is beyond the scope of this report. These factors assist the physician in determining the necessity and appropriateness of radiation therapy and can be used to develop Quality Indicators (QI). QIs can be used to perform peer review or chart checks prior to the initiation of therapy. For example, in a cancer patient, the documented existence of a cancer diagnosis is required by many institutions prior to the delivery of radiotherapy. The presence of a cancer pathology report in the medical record, therefore, can be used as a quality indicator (QI) metric.

These factors generally include but are not limited to 1) type and extent of disease (staging in cancer patients) which often assist a physician determine whether a treatment is palliative or curative, 2) patient factors such as the existence of conditions that increase the Risk of radiation toxicity (scleroderma and other collagen vascular disease), 3) treatment-related factors (prior radiotherapy and use of chemotherapy agents that increase Risks), 4) presence of factors that may be contraindications to or complicate the delivery of therapy (pregnancy, presence of a cardiac device, presence of high Z material), and patient preferences. These factors used to assist the physician in decision-making can and should be adjusted on a disease-specific basis. In addition, these factors should be adjusted for particle therapy compared to photon therapy. For example, the presence of a prosthetic hip in a prostate cancer patient should be recognized prior to making a recommendation about particle therapy given the potential adverse effect of the prosthesis on the dose distribution.

A significant vulnerability in the consultation workflow processes which relates to the AHRQ safety culture survey attributes of communication openness and handoffs/transitions is the incomplete collection of needed information prior to and during the consultation process. It is useful to use develop and use standard forms to ensure that the necessary information is collected. Examples of such forms include 1) pre-consultation data collection form (pathology report, imaging studies, prior medical records), 2) medical history form including a standard review of systems document, 3)standardized physical examination forms, 4) baseline patient-reported outcome measures, and 5)a pre-treatment or pre-simulation checklist.

After the collection of data, interview and examination of the patient, and review of data, it is necessary for the physician to formulate a recommendation regarding treatment part of which will be the prescription. An additional vulnerability in this portion of the consultation is the skill set of the physician and the quality of the overall practice. One example is the lack of familiarity of the physician with evidence-based treatment standards such as the National Comprehensive Cancer Network (NCCN) guidelines which can also be used as QI measures [35]. Also, sometimes, the lack of knowledge of the existence of a protocol and current clinical trials can be an issue. Another example is the importance of standards for physician and practice competence/quality such as board certification, maintenance of certification, and practice accreditation [36]. A particle therapy-specific feature of physician competency assessment is knowledge and experience with the subtleties of particle therapy treatment planning and treatments. It is recommended that institutions have particle therapy-specific credentialing programs which include didactics, hands-on treatment planning sessions, proctoring of initial patient cases by experienced clinicians, rigorous peer review of each patient case, and ongoing peer evaluation of competencies.



After formulation of a treatment recommendation, it is then imperative for the physician to complete the medical record in a timely fashion and discuss the treatment options with colleagues from other specialties in a multi-modality setting. This provides another check on the appropriateness of treatment recommendations. Another vulnerability in the consultation workflow processes which again relates to the AHRQ attribute of communication is the lack of familiarity with particle therapy of colleagues from other disciplines such as surgery and medical oncology. For example, the placement of certain types of hardware or metallic clips may affect the ability to delivery particle therapy. In addition, choices of concurrent chemotherapy may be affected by the use of particle therapy. Multi-modality discussions regarding particle therapy will likely increase acceptance of its use and lead to more appropriate treatment decisions.

A critical part of the consultation process is a complete and understandable discussion of the treatment recommendations with the patient. This should include a discussion of the array of treatment options (e.g. surgery, chemotherapy and radiation) as well as information related to particle therapy and how it differs from other forms of radiation treatments. Standardized patient information guides including online documents or video are often useful to facilitate discussions with the patient and other caregivers.

A graphical representation of the steps noted above is shown to the right. Note that some of these steps, are, in fact, mitigations.

What is NOT included in the above diagram, but was briefly discussed in the text, is the identification of the vulnerabilities and details of the actions in each of these steps.

As an example, one can perform an FMEA with some of the above steps as shown in Table 8.1.1 below.

Table 8.1.1 FMEA examples from about narrative

Step	Failure Mode	S	P	Mitigation(s)
Formulate Tx recommendation	Cancer pathology report is not included	High	Low	Perform Standard evaluation; Create a checklist and/or secondary chart; check (or software)
Formulate Tx recommendation	Existing Clinical Trial is not used	Subjective	Moderate	Discuss with colleagues

8.2 Simulation

The use of CT-based three-dimensional imaging for Radiotherapy simulation is now considered standard. Although there are no prospective Level 1 data demonstrating the impact of CT-based simulation on patient care, some authors have shown a significant impact on patient outcome [37]. Obtaining patient consent is the first step in the simulation process and requires a thorough discussion of the procedures involved as well as the Risks and benefits of treatment. At the time of the consent discussion, patient instructions should be given verbally and in writing. This may include preparation for immobilization devices such as a rectal balloon or oral intake restrictions prior to administration of intravenous contrast.

After obtaining consent, a physician order is placed. Accurate and timely communication of CT simulation parameters is a necessary part of the physician order and includes complementary imaging modalities for fusion (MRI, PET), use of contrast agents, assessment of target motion, patient position, and immobilization devices. The use of a contrast agent may be necessary to delineate the target volume (e.g. identification of the mediastinal lymph nodes in a lung cancer patient) but may also present problems during the treatment planning process for particle therapy as in the potential use of the incorrect calibration curve. Likewise, immobilization devices specific for particle therapy may be required. A vulnerability in the simulation workflow which relates to the AHRQ survey attributes of communications and handoffs is the lack of accuracy and precision of the physician's order particularly as it relates to the specific needs of particle therapy planning. An electronic template with drop down menu choices for physician orders is an ideal way to ensure accurate communication of information. QIs can be developed around the accuracy and timeliness of physician orders prior to simulation.

Scheduling of patient simulation and the subsequent initiation of treatment is typically the next step in the simulation process. A process vulnerability exists because the often complicated treatment planning process may take a longer period of time compared to the process in conventional radiotherapy. Creating a standardized workflow process map with designated timelines is useful to monitor the timeliness of treatment planning and initiation of therapy. QIs may be developed and monitored around metrics such as time from consultation to simulation and simulation to first treatment. As particle therapy experience and usage grows, it is imperative that efficiencies are brought to the simulation and treatment planning process and are made similar to those found with photons. Following QI metrics will assist in that process.

In the simulation process, the physician writes a prescription for particle therapy. Ideally, this occurs prior to the actual simulation as such information could be useful for physicists, radiation therapists, and

dosimetrists during the simulation. Accurate and timely communication of prescription parameters is required and includes location of target, total dose, fraction number, energy, therapy modality, dose parameters for target coverage, and dose constraints for organs at Risk (OAR). A similar vulnerability in the simulation workflow which relates to the AHRQ survey attributes of communications and handoffs is the lack of accuracy and precision of the physician's prescription. An electronic template with drop down menu choices similar to that described for simulation orders is also useful for physician prescriptions.

An additional vulnerability in this portion of the simulation process is the familiarity of the physician with OAR constraints and acceptable doses to the target volume. Evidence-based dosing standards are emerging and provide useful data to populate standard physician prescription templates. Likewise the mandated use of standard nomenclature for OARs and target volumes are likely to reduce communication errors. This is a particularly important issue for particle therapies where uncertainty regarding range and location of higher LET energy deposition may influence choices regarding dosing parameters.

The simulation also provides an opportunity for the physician to determine if other specialized services are needed during the treatment planning process. This may include but are not limited to Special Physics Consults to address issues such as overlap with prior radiation fields, assessment of the fidelity of image fusion, review of cardiac device tolerance limits and the need for comparative planning with photons. One vulnerability in this portion of the simulation process is the variability in the use of Special Physics Consults. Once again, the use of a checklist will assist the physician in determining if any conditions are present which require the request for a Special Physics Consult.

At the time of simulation, the patient is immobilized in a position prescribed by the physician in consultation with physicists, dosimetrists and radiation therapists. A CT scan is obtained and images are reviewed by the physicist and physician and the isocenter is placed. Four dimensional CT scans through all phases of the respiratory cycle are commonly used in the particle therapy setting because of the sensitivity to tumor motion. The use of 4D CT scanning requires assessment by the physicist of the consistency and reproducibility of respiratory motion [38]. The simulation may also involve the use of motion management devices which are likely to increase the complexity of the simulation process. In certain clinical circumstances, the physician may determine that fusion of the CT scan with an MR scan or 18FDG PET scan is needed for more robust target or normal tissue delineation. For the MR and PET scans, patients must be placed in the same position as that used for the CT simulation. Another vulnerability of the simulation process is the size of the error in patient positioning for MR and PET which may translate into less robust image registration and possibly inaccuracies in target and OAR delineation.

A final portion of the simulation process is the contouring of target volumes and OARs which introduces perhaps the greatest uncertainty in the treatment planning process. Multiples studies have demonstrated the inter- and intra-physician variability in target and OAR delineation [39]. The variability in contouring of targets and OARs represents a significant challenge and vulnerability in particle therapy. Methods for standardizing and automating target and OAR contours are emerging and will likely be part of routine clinical practice in the near future [40].

A portion of the process map related to imaging can be visualized according to figure 8.2.1 below from [15]. This figure, rather than being a simple step by step list is a process flow map, complete with decision branches and indicative of the level of detail that is helpful in analyzing the consequences of potential issues. What is NOT included in this, which could be analyzed separately, is the consequence

of a decision element failing. This is perhaps a matter of redundancy and appropriate detection as will be discussed in the analysis sections.

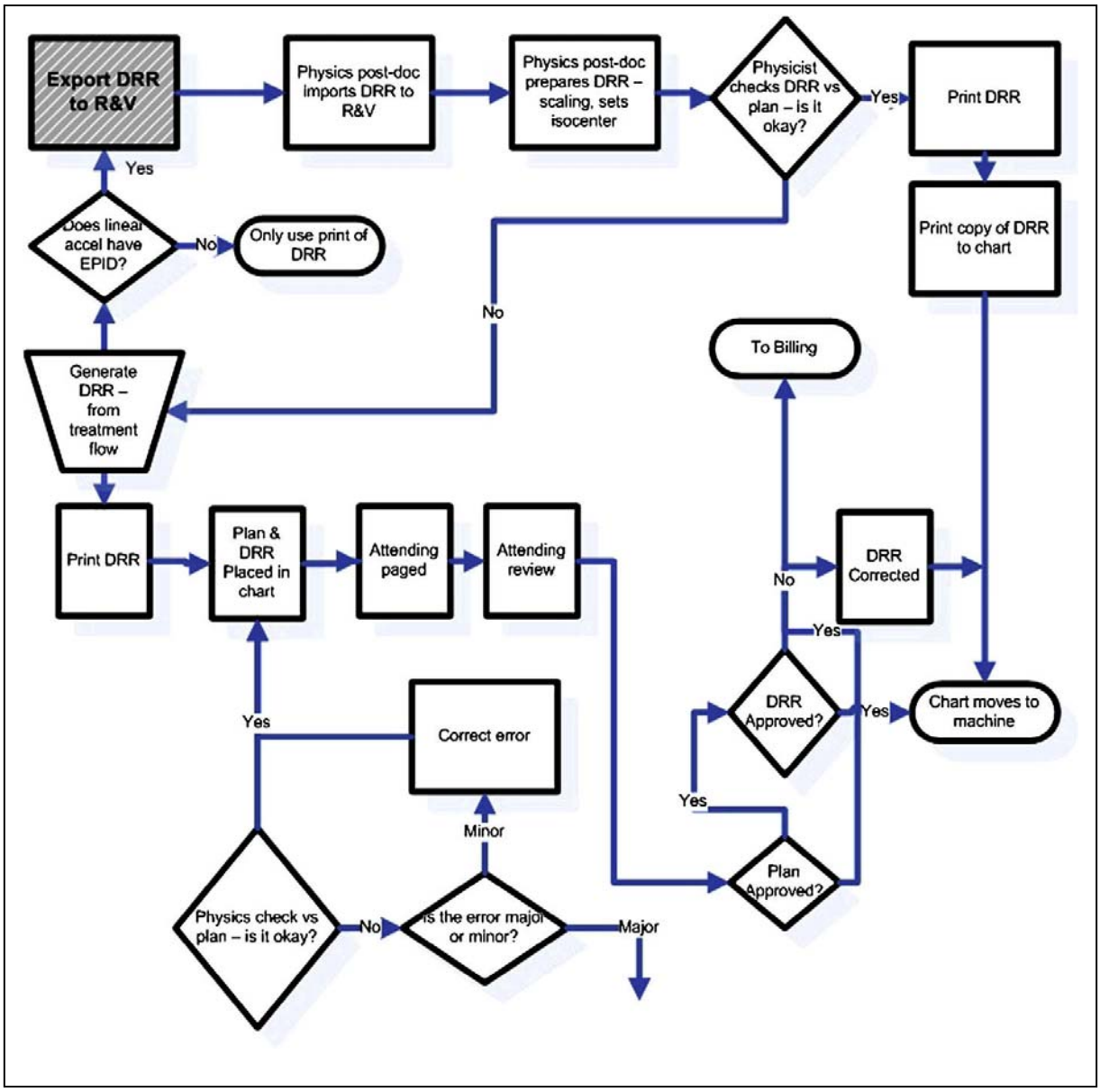


Figure 8.2.1 DRR Export Process Flow Map [ref

8.3 Treatment Planning

Treatment planning may also be different at different institutions and can depend upon the personal preference or even the particular systems used. Previous Radiation Oncology error studies point to treatment planning as one of the most at-risk processes (the data are not great, but it is worth mentioning) [15]. An error in treatment planning can potentially be propagated through the entire course of the patient's treatment. Note that many of the same error pathways exist for particle therapy as exist for photon therapy, but there are indeed some specific to proton RT such as CT imaging protocols, dose prescriptions, range uncertainty and motion in scanned beams.

Since a treatment planning system can be very complex and can be used in many different ways, it is important to define controlled workflows for certain tasks, which may also be documented in standard operating procedures. Furthermore, training of the users is mandatory. This is typically provided to some expert users by the by the manufacturer and subsequent training of all user groups by these experts according to the workflows of the individual facility. Also the software rights for certain steps in the planning process, like e.g. approval of treatment parameters, prescription or treatment plan, etc. should carefully be configured for different user groups. By doing so, the Risk of changes of essential parameters, like e.g. definition of the target volume, can be limited. A general guideline, which is a good starting point to analyze the treatment planning process is given by the International Atomic Energy Agency (IAEA) report "Commissioning and quality assurance of computerized planning systems for radiation treatment of cancer" [41].

8.4 Treatment

Treating a patient involves several interrelated functions. Yet another representation of the process is a "Use Case" diagram shown below. In this type of representation, multiple 'actors' are identified. An actor is a system or a person who has the responsibility to perform, initiate, and react to various parts of the process. In the diagram below (figure 8.4.1), the following acronyms are noted:

- RTT – RadioTherapy Technican (Therapist)
- TCS – Treatment Control System
- PVS – Patient Verification System (Alignment System)
- MCS – Motion Control System

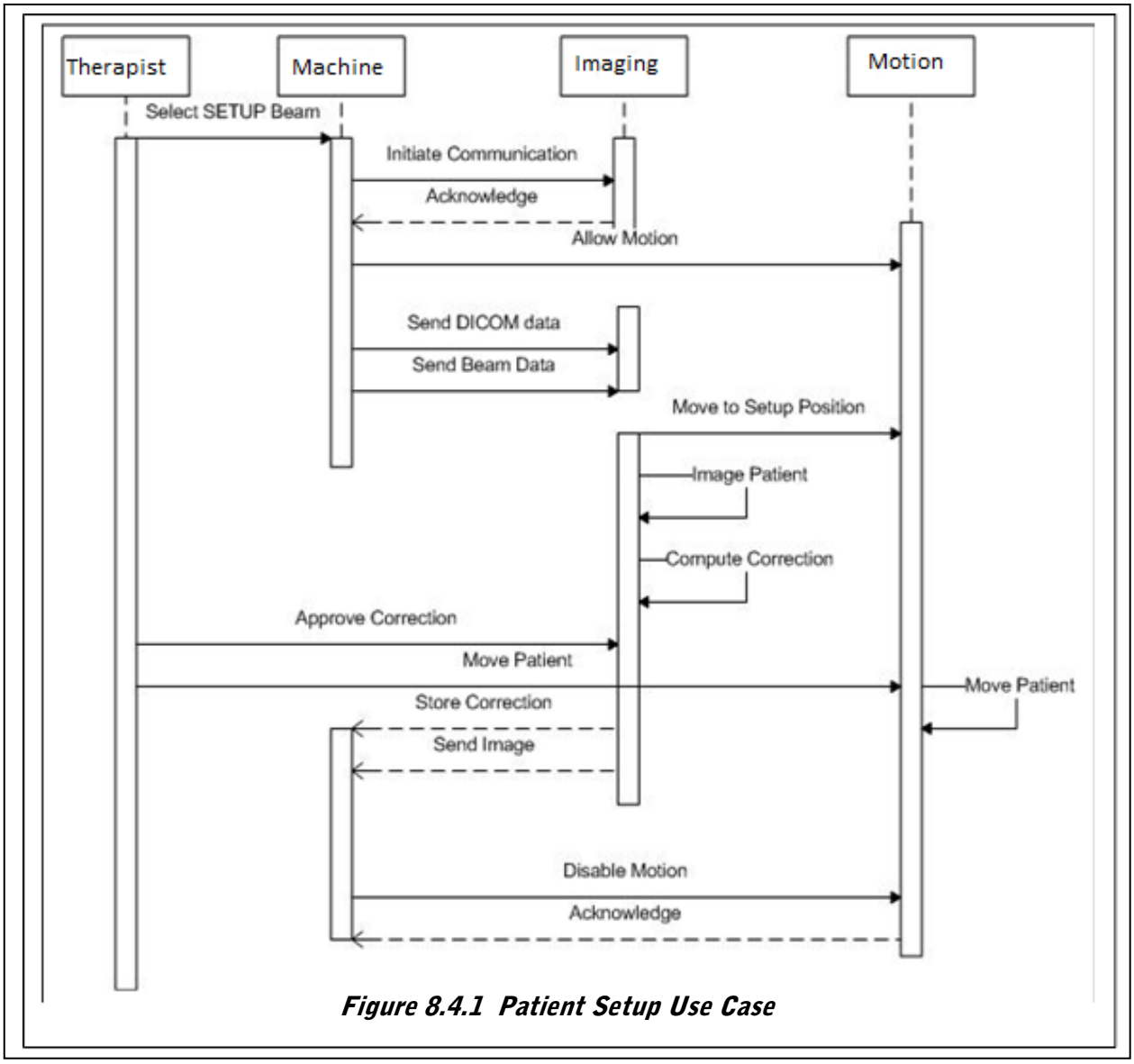


Figure 8.4.1 Patient Setup Use Case

This use case example only shows the portion of the treatment associated with the 'setup' of the patient. It represents a particular example of a distribution of actions which may not be reflective of many existing systems, but it does show how distributed functionality may be arranged. Note, that with distributed functionality comes the necessity to transfer information, which itself is a potential source of error. A diagram such as this, continuing on through irradiation can be developed for the readers system.

9. Quality Assurance

Quality Assurance (QA) is part of the clinical workflow, however for the purposes of this report, it is examined in somewhat more detail than the other process steps perhaps because of the underlying level of detail. The implementation of a Quality Management System (QMS) includes Quality Assurance of various processes. Under the title of QA, virtually any check that the process is correct is part of QA. For example, a check that a patient's chart has the correct data is QA, verification of a patient specific

hardware such as a compensator or block is QA. Perhaps the most detailed QA is the measurement of the beam and verification of beam measurement devices. All of these aspects of QA should be identified in the workflow steps and identified as such. Sometimes it is confusing to determine who is responsible for what, or what function should be analyzed. It is helpful, for example, if QA is incorporated into the QMS and that the responsible individuals ensure that the QA checks are implemented throughout the entire workflow. More generally, QA is defined as the set of all planned and systematic actions in a quality management system, which are necessary to provide confidence that a product or service will satisfy given requirements for quality. While the subsequent subsections focus on aspects of beam quality assurance, the other aspects of QA, described herein should not be minimized. Quality is often limited to measureable performance parameters, like dose accuracy etc. It should, however, be emphasized, that safety is inherently also a quality parameter.

9.1 Beam Quality Assurance

Quality Assurance protocols related to beam measurements include the procedures necessary to provide confidence that a radiotherapy machine can produce the required dosimetric parameters for patient treatment. . In the case of a radiotherapy system beam QA will include the acceptance testing of a system, the clinical commissioning, and finally an ongoing and living quality control (QC) process including machine and clinical QA. It may be helpful to consider that QA (especially with respect to safety) is really an error mitigation scenario. There are some possible failure modes of a system and QA is one method to detect and react to some possible errors.

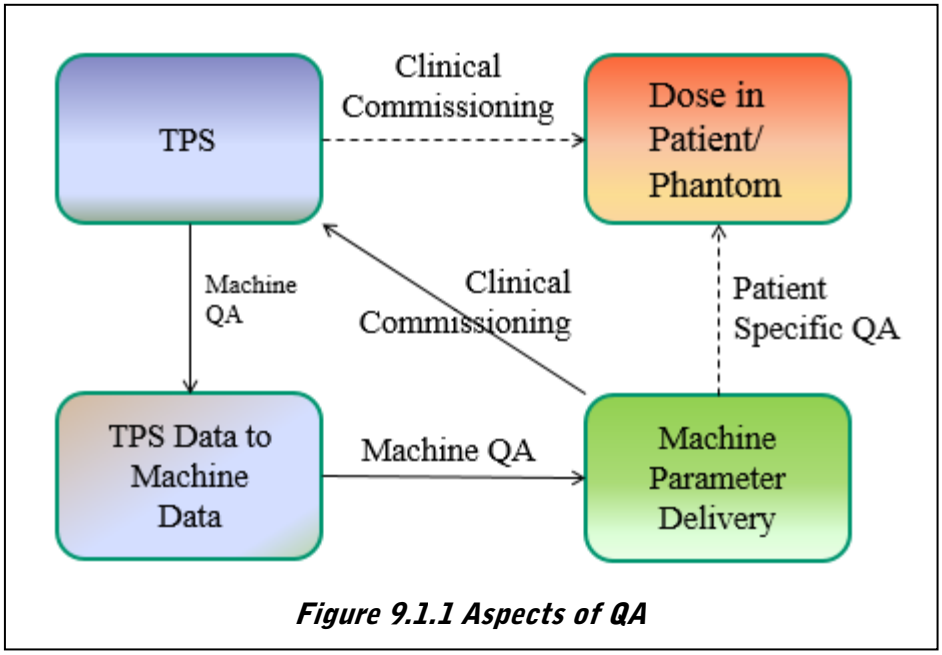


Figure 9.1.1 Aspects of QA

One can define two key branches of QA; one is machine QA and the other is clinical QA. These can be illustrated in the figure 9.1.1 above.

In the case of machine QA (lower yellow box) it is necessary to "assure" that the Proton Therapy System (PTS) machine produces the beam parameters that a Treatment Planning system (TPS) uses to determine the dose distribution. If, for example, the TPS requires a proton beam with a range of 20cm, does the machine produce that proton beam with a range of 20cm (within acceptable margins). In the case of Clinical QA (upper part of figure), it is necessary to "assure" that, using the beam parameters input in the TPS (from the machine), the dose distribution predicted by the Treatment plan is that which

will be delivered. In other words, are the algorithms embedded in the TPS correct (not asking the question of whether the beam produced by the machine is correct, or the parameters have been transferred correctly)? Getting the correct beam parameters into the Treatment Planning system is sometimes called "Clinical commissioning" (left hand and upper part of figure), not to be confused with "Machine commissioning" which works towards obtaining the desired machine beam parameters. Both should be considered to be part of a more general commissioning process, which aims at providing all necessary procedures, protocols, instructions and data to start clinical service (which includes by itself the development of QA procedures).

There are many things which might be considered for measurement as part of the QA process. One should apply the analysis techniques discussed in this report to help determine the necessity and frequency of the measurement. One can make measurements of the components of the equipment to ensure that they are operating correctly, which is a reasonable thing to do. However, in the end one is hoping to assure that the beam parameters delivered by all the components comprising the equipment, is what is requested. If one concentrates on this aspect of measurement one is basically focusing on the dosimetry beam quantities. It is possibly helpful to separate the so-called "dose distribution" into three categories:

1. The absolute dose
2. The relative distribution of a dose
3. The absolute position of the dose distribution

In this way, one can more easily separate out those parts of the system that must be verified as part of the dosimetric QA process.

Following from the above logic, machine QA can be defined as the act of checking that the system produces the same parameters as when it was measured for clinical commissioning, and patient QA can be defined as the act of checking the treatment plan (TP) output for a specific patient plan. Of course if the TP implementation is perfect the two are the same, but patient specific QA must be done when it may be that a specific patient plan could introduce an aspect of the planning which may not have been previously exercised (such as heterogeneities), or it involves a combination of machine parameters, which may be critical. When applied to the machine, the patient specific QA verifies that the machine produces the dose distribution that the TP predicted.

9.2 Clinical and Machine parameters

In general, when considering the analysis techniques to be described in the following sections, it is necessary to collect the information that will expedite the work. At the highest level, one needs the requirements such as the three categories of "dose distribution" that were defined in the previous section. Once one understands these requirements, one should identify the consequences of not achieving them and the tolerances associated with them. In the topic of beam QA a parameter (such as beam range) can have a tolerance associated (such as $\pm$0.5mm), but in other aspects of clinical workflow, such as using a CT image, there may only a binary right or wrong image. (Of course, analyzing that image, however, includes converting the CT densities obtained to proton beam stopping power (for example) which has in itself inherent uncertainties.)

Figure 9.2.1 below shows the dosimetric regions of interest for the two key beam delivery methods, double scattering (left) and scanning (right). This is essentially the 2nd item in the dose distribution category list identified in the previous section. There are other beam spreading methods, and this highlights the need, for each delivery method, to identify the crucial parameters that characterize the dose distribution.

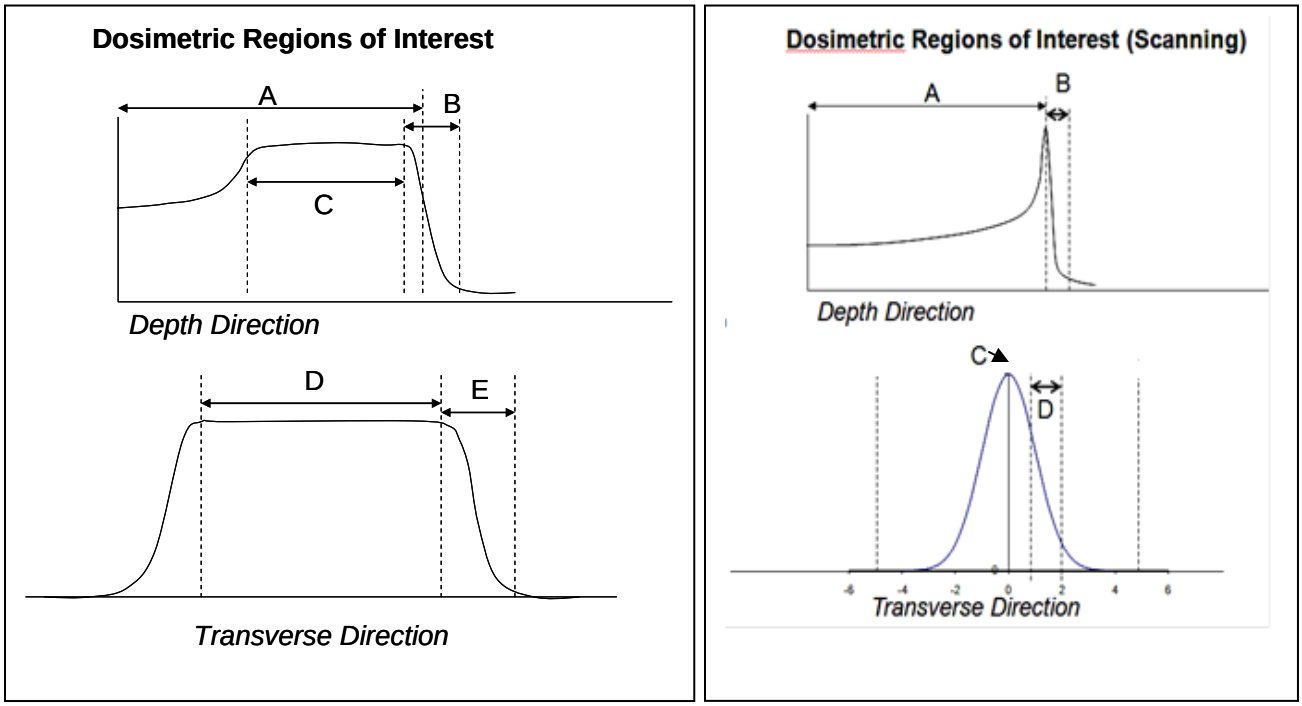


Figure 9.2.1 Dosimetric quantities for scattering and scanning beams.

In the figures for scattering the following parameters have been identified:

A. The Range of the Spread Out Bragg Peak
B. The Distal Falloff or Distal Penumbra
C. The Width of the Spread Out Bragg Peak
D. The Transverse Uniformity
E. The Lateral Penumbra

In the case of Scanning, the beam is unmodified and therefore the relevant beam parameters include:

A. The Range of the pristine Bragg peak
B. The Distal Falloff or Distal Penumbra
C. The centroid position of the beam and its stability
D. The lateral penumbra, which is related to the beam size and shape

Another useful quantity for treatment delivery is the relationship between the entrance dose and the dose monitor readout (sometimes referred to as monitor units or proton charge delivered). This parameters will normally be measured at different locations and different gantry angles if gantries are involved.

These parameters are tagged because they can represent the relevant beam parameters created by the beam delivery system and are used by the Treatment Planning systems to calculate the dose

distribution. Also, they represent a further breakdown of the requirements needed to identify the types of potential errors that may arise in the beam delivery.

The definitions of these parameters may be varied and have to be clearly specified. For example, at which position the range is defined or the distal fall-off is measured. In principle, there may also be additional parameters, like e.g. the roundness or symmetry of a beam centroid.

Table I in Appendix A includes these parameters as the key dosimetric beam parameters that may be measured during QA procedures.

Once these clinical beam parameters are identified for the beam delivery method, it is helpful to determine how these parameters are created. For example are there magnetic focusing elements used to define the beam shape, or are there physical beam modifying devices in the path of the beam? This information, once acquired, then allows one to identify the equipment used to generate the clinical beam, and in turn, identifies the equipment parameters that may be measured as part of the QA procedures.

There is clearly a difference between measuring clinical beam parameters using external instrumentation and measuring the status of a piece of equipment which may uniquely determine that beam parameter. Determining the relevant measurement is part of the process of designing the QA procedure. Often both measurements may be done consecutively during commissioning in order to relate them to each other.

For the double scattering example we can go through that exercise for a particular system.

A. The Range of the Spread Out Bragg Peak: In this case, the Range is primarily determined by the range of the most distal Bragg peak (although there is a component of the next proximal peak that contributes).
    a. This range is primarily determined by the beam energy.
    b. In addition, the beam energy is modified by materials that the beam traverses including, for example:
        i. Scattering devices
        ii. Range modulating devices
        iii. Vacuum to Air transitions
        iv. Instrumentation material
        v. Etc.
B. The Distal Falloff: This is determined by the final energy spread in the beam which is comprised of the following:
    a. The initial energy spread in the beam.
    b. The range straggling created when the beam traverses material before entering the target. (See A.b. above.)
    c. The range straggling created when the beam traverses the target.
C. The width of the spread out Bragg peak: The SOBP is generated by combining the appropriate number of Bragg peak by some method.
    a. The devices used to modulate the Bragg peak such as a range modulator wheel, or binary filters or ridge filters.
D. The Transverse Uniformity: This results from a variety of devices:
    a. Scattering material
    b. Collimator

c. Air gap between collimator and target
d. Distance between effective source and target
e. Beam Centering

E. The Lateral Penumbra: This also results from a variety of devices
a. Collimator
b. Air gap between the collimator and target
c. Effective source size
d. Multiple scattering in material and the target

The above is an example. Each system can be so analyzed in more detail. What is interesting, is that in this example for scattering, the only parameters in the original beam (from the accelerator and beam line) that are relevant are the Energy and Energy Spread. These are the components that affect the beam parameters mentioned. That is not always the same as the parameters that 'control' what the beam parameters may be. For example, the above list does not include the magnetic bending dipoles. Depending upon their setting (in some systems – not all) the beam energy transported to the treatment room will be determined. These do not adjust the beam energy, they only select which energy is transported. Verification of this type of control element or verification of the other elements which actually affect the beam energy are options when considering error analysis and the QA to be performed to mitigate possible errors.

Note that in the case of scanning, since the beam is unmodified, the parameters that are to be measured are the same parameters as shown in the above figure. A key addition to this is the effect of the scanning system including any modification to the beam size and position as the beam is moved across the target. Some scanning systems allow for a variation of beam width, which in combination with variation of energy, may lead to a substantial number of combinations that may have to be checked. These are aspect of how interlocks are configured and should be subject to a Risk analysis.

Thus the clinical beam parameters can be related to the beam parameters through the equipment used to spread out the beam. Identification of this equipment can help to start a failure mode analysis.

9.3 How often to measure?

From the perspective of process steps, this is a question of how often to perform a particular activity/check. For example, is the CT scan the correct one. There are a variety of steps which require the use of a scan, from diagnosis to planning to patient setup. Should they be checked at every step, should they be checked every day even though a step being executed does not use the scan. This will be related to the Severity of the potential Hazard of not doing the check. Also important is to ensure that the check (the mitigation) will result in a low Probability that, when used, will not detect the wrong scan. In the latter case, the check is not an appropriate one.As an example, one may think of a check of the accuracy of the Hounsfield units (HU) in a treatment planning CT. This can be done e.g. with real measurements and high accuracy in dedicated phantom. Simple automated checks which may involve either test objects in the images of each patient, or an analysis of the overall HU-distribution in each patient CT, may allow to drastically reduce the frequency of more time consuming measurements.

From the equipment perspective, it is not enough to identify all the parameters and equipment that can affect the desired beam delivery. One also asks how often a parameter needs to be checked. This is determined by analyzing the Severity of the failure of this parameter to meet a desired value and the Probability that such an event will occur. This analysis could be included in a Failure Mode, Effects and Criticality Analysis. All too often, QA procedures from one machine to another follow some standard

which may not be relevant to the specific nature of a given machine. The question of who should identify these unique situations is not addressed here, but the fact that these should be understood to guide the design of a QA process is clear.

Clearly, potentially serious failures, such as overdose are monitored very often independent of the Probability of its' occurrence. In such a case it's almost as if the RPN were determined solely by the Severity number. In fact it is monitored in real time during a radiotherapy treatment. In addition, the instrumentation which performs this monitoring is checked daily during physics QA of the machine. Thus the question of what can and should be monitored in real time versus less frequently is posed. In addition, the device that is used to measure something in real time may fail and therefore a frequency of verification of that device must also be factored into QA procedures. Some time intervals include:

1. Real Time or On-line
2. On-line initial check just prior to treatment
3. Daily, Weekly, Monthly checks
4. Annual Checks

Table 1 of Appendix B summarizes the clinical beam parameters and some hardware parameters for Scattering and Scanning and identifies an example of the frequency of each of these measurements. The decision for these is system dependent and it is not expected that this example should be implemented without a thorough individual evaluation. Once again the particular implementation will depend upon the type of equipment used. For example, in the case of scattering, a ridge filter is a passive device that is unlikely to fail, but in almost all other cases, scattering is NOT a passive modality and there is various moving equipment or equipment whose timing must be verified and it's possible that this equipment, or the beam produced by this equipment should be evaluated more often. The following is an example of a sort of Hazard analysis that helps to identify the frequency of measurement for some situations.

High Level Beam Property	Specific Beam Property	Severity of Hazard		Probability of Affecting									Product of Probabilities	Normalized Probability		RPN Product		Mitigation Type Possible?
				Incident Beam Trajectory	Intrinsic beam energy spread	Incident Beam Size	Energy Degrader	First Scatterer	Second Scatterer	Collimator	Compensator							On-line measurements
Beam Range																		
	Beam Range Value	**3**		1	1	1	3	2	3	1	3		54	0.37		1.13		No
	Range Spread	**2**		2	2	1	2	1	3	1	2		48	0.33		0.67		No
	SOBP Uniformity	**1**		2	2	1	2	2	3	2	3		288	2		2		No
Beam Profile																		
	Field Size Values	**3**		1	1	2	2	2	3	3	2		144	1		3		Yes
	Field Uniformity	**2**		3	1	2	2	2	3	3	2		432	3		6		Yes
	Position Values	**3**		1	1	1	2	1	1	3	2		12	0.083		0.25		Yes

There are many numbers in the above table. This is the result of a subjective analysis, but perhaps the thinking behind some of these numbers can be reflective in the thought process used to determine the relative Risks and resulting frequency of measurement. Some of the clinically relevant beam parameters (see figure 9.2) are listed. The effective 'hazard' is that the specific beam property (2nd column) is not what was prescribed. There is no indication of why that happened or the failure mode yet. In the next column the 'Severity of the Hazard' is tabulated (see e.g. section 5.4). So, for example, if the beam range is incorrect this can result in an overdose to the normal tissue and/or an underdose to the target, both very severe consequences. In this table, the scoring is 1 to 3, where 3 is a worse case (very severe or highly probable). The range spread is not good, but for most cases of the types of errors possible, the spread will not cause a problem as severe as a wrong specific range. The hazard of inappropriate uniformity is not typically as severe as other errors. But it may be argued that it can be, and therefore should be more severe and that the probability should contain this information. Regarding the transverse beam properties, the field size and position will play a major role in the incorrect dose distribution, as could the field uniformity, but that will have less of an effect typically. One can, alternatively take the worst case scenario and score 3 for all of these, but that is left as an exercise to the reader.

The next set of entries include some specific causes or items that will affect the particular beam parameter in a double scattering system. There are many system dependent considerations factored into the above numbers:

- For a double scattering system, the input beam trajectory has less of an effect on the field position and size due to the use of a collimator, but is has a strong effect on the transverse field uniformity due to the effect of a non-uniform second scatterer.
- The effect of the initial beam energy spread has less of an effect on the transverse parameters than on the distal fall-off. The latter will have an effect on the SOBP uniformity.
- The energy degrader will have a major effect on the beam range and the beam range will play a role in the transverse beam parameters, but the latter will depend upon the quantitative amount.
- The second scatterer, especially a rotating second scatterer can have various failure modes and strongly affects both the beam range and the transverse scattering
- The collimator position and possible edge scattering effects will play a major role on the beam transverse properties and owing to the scattering possibilities, also affect the SOBP uniformity.

There are two columns summarizing the Probability result. One is the raw product of all the probabilities in a row, and the other is normalized so as to force the maximum Probability to be 3, so as not to overwhelm the RPN=SxP product. The Probability of a particular Hazard will be related to the product of all of the probabilities of the individual faults that can occur. This Probability, it is important to understand, is BEFORE any further mitigation. Note that it is most probably to achieve an error in transverse field uniformity, followed by an error in SOBP uniformity. However, the highest RPN numbers go from transverse uniformity to transverse field size, to SOBP uniformity.
One may reason that one should use the RPN numbers to determine the level of Criticality and the mitigation. In addition to hardware and controls mitigations to ensure that the scattering and beam related components behave as desired, one implements a functional redundancy (see section 7.2.4) which facilitates the on-line (during treatment) measurements of certain beam properties. The transverse beam field size and uniformity are relatively easy to measure, but the SOBP uniformity is not easy to measure on-line. The conclusion may then be that the SOBP uniformity should be measured

more often than the other parameters which have mitigations (on-line measurements) to further reduce the Probability.

Alternatively, one can consider another strategy. Independent of the Severity of the Hazard, one might look at each of the potential failure modes components that have a level 3 Probability. This would include

- Incident beam trajectory
- Energy Degrader
- Second Scatterer
- Collimator
- Compensator

One would then ensure that these components themselves are monitored through quality assurance and/or ensure that the QA program includes measurements to confirm that they are behaving properly. This results in a Patient Specific QA program to inspect the collimator and compensators before the first use, and beam measurements at various energies to ensure that the beam parameters are correct. The latter can be hardware specific (e.g. create a short beam pulse to generate a specific pristine Bragg peak on a moving range modulator wheel) or be more general and measure an output factor.

At the very least, discussion of the numbers applied to the above table, can help the analysis team better understand their system and create a safer treatment process.

10. A Shared database for safety and quality improvement

The above sections have presented a few examples of possible Risk scenarios in proton radiotherapy. It is beyond the scope of this document to provide a comprehensive list of possible error pathways, nor would such an exercise be advisable since technology and processes change rapidly in this field and since error scenarios will depend so much on the particular clinic in question and the equipment, policies and procedures that are in place.

Nevertheless, there is a clear need to share information about possible between clinical users. One of the major flaws of prospective Risk assessment such as FMEA or the like is a "failure of imagination", i.e. the inability to identify and recognize possible Risk scenarios. Sharing experience among clinics is a step toward addressing this. The concept is similar to that used in the commercial nuclear power industry. Each day an alert is sent out to all plants by the Institute for Nuclear Power Operators, INPO, an industry-supported organization. These INPO alerts identify a handful of conditions that have been identified at one plant that may be relevant to other plants.

For these reasons we believe a shared database of possible Risk scenarios may an advantage to those who wish to further improve the quality and safety of clinical operations. The database would serve as a clearinghouse for possible Risk areas and would be entirely anonymous.

As a starting point also an institutional system may be established that allows so-called *blame free reporting* of critical events not necessarily leading to an incident. These systems are also known as *critical incident reporting systems* or CIRS and may serve as an important input for further improvement of Risk mitigation and quality management.

Outline of some issues to discuss:

- Note this is different than actual 'incident reports' which describe actual or near-miss events that may have affected a patient. This database would be restricted to hypothetical Risk scenarios. This gets closer to the AHRQ's use of 'unsafe condition' reports. This obviates the many issues related to reportable events.
- Does this data need to be protected from discovery? If so, then the Patient Safety provides a mechanism for this. ASTRO and AAPM have contracted with a PSO organization (Clarity Group) to provide PSO-enabled services for the purpose of incident learning under the Radiation Oncology Incident Learning System: RO-ILS ™, launched in June 2014 (astro.org/roils)
- Database structure can be discussed more and fleshed out. One basis could be the white-paper from AAPM recently released in Medical Physics [42] It specifically describes the structure of incident reporting databases, but much of the same structure would apply. I imagine a common process map that can serve as a generic template (there is something already in the AAPM white-paper that may be relevant). That would provide a structure around which FMEA scoring could be performed. Note there are some commercial FMEA systems available which appear quite good.
- The database could be seeded with hypothetical error scenarios. There should be some QA and oversight on the data coming in. There should be an anonymous way to get back to the contributor to clarify descriptions or other issues.

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12. Table of Figures

13. APPENDIX A: Acronyms and Definitions

Indeed there are a number of terms that are useful to consider in this endeavor.

Term	Meaning
Criticality	An evaluation of the importance of a Risk
Event Tree	Starts from a mitigation of an effect of a failure and then walks down the path of those issues that can prevent that safety mitigation from working
Fault Tree	A top-down approach. One identifies a chain of events starting with an accident or Hazard or fault and identifies Hazards that may contribute to that accident
FMEA	A bottoms-up approach. Failure Mode and Effects Analysis: An analysis of the possible failure modes and what effects they would have, their importance and how to mitigate these effect
Hazard Analysis	At top-down approach. An evaluation of the kinds of Hazards that are possible, the Risks involved and an analysis of their importance and mitigation.
Mitigation	Something used to reduce the Risk of a Hazard or Failure
Risk	A combination of the Severity and the Probability of an event
Workflow	The steps (not necessarily in any given order) required to perform a treatment

14. APPENDIX B: Beam QA Frequency Example (Possible implementation)

			SOBP						PBS								Range of Values Used for the testing				
			Measure On-line Values	Measure On-line Settings	Measure Daily QA Values	Measure Daily QA Settings	Measure Less Frequently		Measure On-line Values	Measure On-line Initial Check	Measure On-line Settings	Measure Daily QA Values	Measure Daily QA Settings	Measure Less Frequently		Gantry Angles	PPS Positions	Ranges Tested	Patterns Tested	Currents Tested	Doses Tested
Depth Dose Characteristics																					
	Energy (Range)																				
		Range Values	Yes	Yes	Yes		Yes/No			Yes?	Yes	Yes		Yes/No							
		Range Accuracy	?	Yes	Yes		Yes/No			Yes?	Yes	Yes		Yes/No							
	Energy Spread (Distal Fall-off)																				
		Energy Spread Values	No	Yes			Yes/No		No	No	Yes			Yes/No							
		Energy Spread Accuracy	No	Yes			Yes/No		No	No	Yes			Yes/No							
	Mod Width		No	Yes					No	No	Yes										
Cross Field Characteristics																					
	Beam Profile																				
		Size Values	Yes (IC1)	Yes					Yes		Yes										
		Setting Accuracy	Yes	Yes					Yes		Yes										
		Gaussianess	No	No					Yes		No										
	Beam Position																				
		Position Values	No	Yes					Yes		Yes										
		Position Accuracy	No	Yes					Yes		Yes										
		Time to get at Position																			
	Beam Velocity																				
		Velocity Values	n/a	n/a					Yes		Yes										
		Velocity Accuracy	n/a	n/a					Yes		Yes										

	Field Size		Yes	Yes			Yes/No		Yes		Yes			Yes/No							
	Field Uniformity		Yes	Yes			Yes/No		n/a		Yes			Yes/No							
	Field Conformity		n/a	n/a					Yes		Yes										
SAD			No	No					Indirect		Hardware										
Dosimetry																					
	# Protons																				
		Intensity Values	Yes	Yes					Yes		Yes										
		Intensity Accuracy	Yes	Yes					Yes		Yes										
		Integrated Fluence Values	Yes	Yes	Yes		Yes/No		Yes		Yes	Yes		Yes/No							
		Integrated Fluence Accuracy	Yes	Yes	Yes		Yes/No		Yes		Yes	Yes		Yes/No							
		Dark Beam Current	No	No					Yes?		Yes?										
		dI/dt	Yes?	Yes					Yes?		Yes										
	Irradiation Time										Yes	Maybe									
		Set Range Time												Yes							
		Layer change time												Yes							
		Time per Layer												Yes							
	Number of Paintings													Yes							
	Gamma Index											Maybe		Yes							

15. APPENDIX C: Hazard Topics

Help identifying Hazards: prEN 1441

- **ENERGY Hazards**
  - electricity
  - heat
  - mechanical force
  - ionizing radiation
  - non-ionizing radiation
  - electromagnetic fields
  - moving parts
  - suspended masses
  - patient support device failure
  - pressure (vessel rupture)
  - acoustic pressure
  - vibration
- **BIOLOGICAL Hazards**
  - bio-burden/bio-contamination
  - bio-incompatibility
  - incorrect output
  - incorrect formulation
  - toxicity
  - (cross-)infection
  - pyrogenicity
  - inability to maintain hygienic safety
- **ENVIRONMENTAL Hazards**
  - electromagnetic interference
  - inadequate supply of power or coolant
  - restriction of cooling
  - likelihood of operation outside prescribed environmental conditions

  - incompatibility with other devices
  - accidental mechanical damage
  - contamination due to waste products and/or device disposal
- **HAZARDS RELATED TO THE USE OF THE DEVICE**
  - inadequate labeling
  - inadequate operating instructions
  - inadequate functional specification for operation of the computerized control system
  - over-complicated operating instructions
  - unavailable or separated operating instructions
  - use by unskilled personnel
  - use by untrained personnel
  - human error
  - insufficient warning of side effects
  - inadequate warning of Hazards likely with re-use of single use devices
  - incorrect measurement and other metrological aspects
  - incorrect diagnosis
  - erroneous data transfer
  - misrepresentation of results
- **HAZARDS ARISING FROM FUNCTIONAL FAILURE, MAINTENANCE AND AGEING**
  - inadequacy of performance characteristics for the intended use
  - lack of specification for maintenance
  - inadequate maintenance
  - lack of adequate determination of end of device life
  - loss of mechanical integrity
  - inadequate packaging (contamination and/or deterioration of the device)