In-Vivo Treatment Verification (IVV): A "Big Data" Multi-center Analysis of More Than 6 Million Fractions Delivered

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Abstract

Purpose/Objective(s): Safety is paramount in external beam radiotherapy. Portal dosimetry with in-vivo verification (IVV) during treatment for every patient and every fraction is clinically feasible on a scale of "big data". Herein, we examine IVV employed for more than 6 million fractions delivered, assaying rates of improvements on treatment consistency, workload needed, and action items triggered per anatomical site.

Methods and Matherials: A multi-center IVV program was implemented in 84 centers over 3 years. More than 6 million daily fractions were recorded and analyzed. For every patient and every fraction, a calibrated portal exit dosimetry panel collected exit beam dosimetry. The average 5-day fraction exit dosimetry panel was compared against a reference fraction using the gamma metric. A "troubleshoot procedure" was used to evaluate the action level threshhold.

Results: In a period of 1 year, delivery consistency metrics improved by 6% for linacs and 7% for TomoTherapy; subsequent results were maintained at post-implementation levels. The level of intervention was significantly dependent on anatomical site. Head and neck, lung, and breast treatments together represented approximately 20% of the total number of action levels that required verification during treatment. In addition, pelvis and prostate represented 13% and less than 10% respectively. Thus, on average between one and two average weekly exit dosimetry portals per patient needed to be verified.

Conclusions: IVV was successfully used to assess lack of consistency on exit dosimetry in more than 6 million fractions across 84 clinics. These data suggest that significant improvements in treatment consistency can be obtained and maintained by using IVV on a daily basis. The high number of flags detected for common anatomical sites was significant and suggests consideration of IVV for every patient with every fraction. Ultimately, this will imply an extra workload leading to future efforts to further optimize IVV procedures.

1 - Introduction

External beam radiotherapy is a commonly used technique to treat cancer. During the last 20 years, radiotherapy has rapidly evolved from three-dimensional conformal radiotherapy (3D) [1], to intensity modulated radiotherapy (IMRT)[2,3], incorprating many forms of image-guided radiotherapy (IGRT)[3]. These technologies aim to minimize the radiation deposited to normal tissues and maximize the dose delivered to the tumor. All of these techniques feature comprehensive quality assurance procedures (QA) that have evolved concurrently with the technology[4-10]. Despite current comprehensive QA programs, incidents may still occur during treatment delivery[11-23].

Classically, IMRT QA can involve either measurements using a phantom as a patient surrogate, or delivery of the plan to a portal imager[9]. Both techniques are typically performed prior to patient treatment. IGRT is typically performed by obtaining portal or CT images, depending on the machine capabilities. Not only do these images aid in patient setup, but they can also be utilized for in-vivo verification (IVV).

IVV is defined as the use of specialized devices on the treatment machine, such as detectors, encoders, monitor chambers, etc., to collect data generated during treatment.

IVV may provide significant insight to evaluate the actual course of treatment vis a vis its predicted progression, potentially detecting previously unnoticed treatment problems or areas for improvement [24-26]. Both France[27] and the UK[28,29] have government recommendations for in-vivo dosimetry techniques. Advances in portal dosimetry for modern machines render in-vivo dosimetry efficient in the modern clinical setting, [24,30-38], though its use may be precluded for select patients, or for those treated with older technology.

A great deal of resources and technology have been invested in pre-treatment QA; however, less attention has been given to QA during treatment, which is of paramount importance. Even efficient techniques to perform IVV increase the necessary workload but provide key information to evaluate and, if necessary, adapt the course of treatment.

2 - Materials and Methods

2.1 - In vivo verification technique

In order to analyze the delivery *during treatment*, a delivery consistency procedure was implemented. Figure 1 is a workflow diagram of the implemented procedure. For each patient and each fraction, a portal image of the transmitted treatment beam is acquired during treatment. This procedure does not imply any extra dose to the patient; the technique only collects radiation going through the patient as a result of their normal treatment delivery. The exit detectors for the linacs had been calibrated following manufacturer procedures to yield readings in Calibrated Units (CU)[35,39,40]. For the TomoTherapy machines, the projection average raw data of the exit detector was used.

Patient setup for all deliveries was image guided, either with portals, CBCT or MVCT. All TomoTherapy patients' setups utilized daily MVCT. The user selected a particular portal as reference fraction. This approach is valid provided that the setup for that reference fraction is adequate and that the anatomical changes between the plan and actual fraction are small. A detailed verification of the registration at the time of treatment for the initial two fractions was conducted, and, when CT was available, the similarity of the anatomy between the planning CT and daily CT was checked. One of those fractions was chosen as the reference fraction if the information was consistent. If the first two fractions were not consistent, set procedures were followed to evaluate possible causes of the inconsistency and to continue the process of selecting a reference fraction.

Once the reference fraction was selected, it was compared against a computed five day average of the daily portals. To compare the consistency between the reference fraction and the weekly average, the Gamma metric was used[41]. Each clinic was allowed to choose their action levels for review: either 3% 3mm or 5% 5mm for the linacs. In TomoTherapy 3% 3mm was always employed.

If the gamma anlysis violated a certain threshold, an investigation was performed to identify and rectify the possible issues. Figure 2 is an example of the table used during the "troubleshoot procedure," which includes a systematic review and an area to indicate the possible cause of failures determined after investigation. Such an intervention is warranted if physician or physicist input is needed.

2.2 - Data sets

Data were collected for 84 clinics over a period of 3 years. The data for linacs are described in Figure 3. 6,465,085 daily portals were analyzed, corresponding to 1,293,085 weekly portals. For this data set, known variables include both the criteria type used by the clinic, 3% 3mm or 5% 5mm criteria, and whether the number of portal points passing that gamma criteria was over 95% or 90% respectively. For approximately 4,309,000 daily portals, corresponding to 861,872 weekly portals, ICD9 information was available to determine anatomical location. For approximately 1,294,000 fractions corresponding to 257,858 weekly portals, the criteria type and exact percentage of points of the portal imager that pass the corresponding Gamma criteria are known. The data set for TomoTherapy contains 42,866 daily portals.

IVV intervention flags due to action level violations were monitored and evaluated for individual anatomical sites. The intervention may correspond to possible setup, machine, or anatomical changes.

3 - Results and Discussions

IVV was successfully used to assess exit dosimetry consistency in more than 6 million fractions across 84 clinics. Figure 4a demonstrates the distribution of anatomical cases analyzed for linacs. Prostate, head and neck, breast, pelvis and lung encompass the majority of portals analyzed. As mentioned, clinics were allowed to choose their action level for review; some used gamma criteria 3% 3mm, while others chose 5% 5mm. In certain cases, select centers switched from 3% 3mm to 5% 5mm during the last part of treatment. Cases meriting this change included patients with significant anatomical changes and/or weight loss that that would significantly alter treatment setup. To further investigate the impact of using 3% 3mm or 5% 5mm as the action level, we analyzed the distribution of the percentage of points passing each criteria. At first glance, two distinctive regions can be observed in Figure 4b. The first region (under 80% threshold) corresponds to system issues such as incomplete image capture, couch bar on the exit beam, incomplete delivery, etc. The region with percentage pass over 80% represents deviations linked to the clinical evolution of treatment. For this region the distribution of points passing the 3% 3mm and 5% 5mm criteria is very similar. The number of cases under the 80% pass criteria is small and decreases very rapidly. This seems to indicate that while it may be desirable to improve quality by working with the tighter criteria of 3% 3mm, major relevant clinical issues are still likely to be flagged with a 5% 5mm criteria.

Next, we analyzed the improvement in the percentage of points passing the action level criteria conferred by IVV from 2009 to 2012. (Figure 5). The percentage of pass, month by month, is displayed for each year in each plot. A significant shift toward higher percentage of pass (on the order of 6% on average for bins between 80 to 95%) can be observed. In subsequent years the improvements were small and reached a plateau. IVV noticeably improved the consistency of the plan delivery and maintained it over time.

Figure 6 displays the percentage of average weekly portals that passed the action level criteria for each of the anatomical sites considered. The data were analyzed separately for linacs (Figure 6a) and TomoTherapy (Figure 6b). Some linac cases were aligned daily by portal imagers; others with cone beam CT. All TomoTherapy cases were CT guided with 3% 3mm tolerance. For head and neck cases 18% of the weekly in-vivo verification gamma in linacs and 22% of the weekly gamma for TomoTherapy triggered action levels for review. As a consequence, one to two weeks of treatment, on average, required a physics review to verify the adequacy of treatment. For the pelvis, 13% of linac and TomoTherapy cases require weekly portal review. For breast, 26% in linacs and 16% in TomoTherapy. In lung, 21% in linacs and 16% in TomoTherapy. For prostate, 11% in linacs and 4% in TomoTherapy. By no means is the lower trigger percentage in TomoTherapy associated with better treatments in that cohort. For breast cases the differences are associated with the flash region, which linacs have but TomoTherapy does not. An action level may be triggered if the breast is in a region outside of the flash region, though this does

not correlate to a clinically relevant issue. In a few linac cases, the retractable arms interfered in different fashions with the exit beam, resulting in a clinically irrelevant consequence. For prostate, lung, and pelvis, the difference between TomoTherapy and linacs is associated with interference from the couch and moveable arms at the exit beam. To eliminate these issues in the future, the threshold for flagging should be adapted for each anatomical site in question.

On average, one weekly portal for every two prostate patients needed to be reviewed. For head and neck, pelvis, breast, and lung, at least one, sometimes two, weekly portals per patient triggered action for review. Clearly, different anatomical sites will need different level of controls during treatment. However, it is important to notice that every patient and fraction needs to undergo review in order to predict which patients will need review, and when. Figure 6c shows the average number of interventions needed as a function of time for all of the anatomical cases analyzed. Around 6% of all weekly patient portals will need review on average. That average number of portal reviews is clearly influenced by prostate cases, since these were the majority of cases evaluated (see Figure 2), and because prostate on average needed less attention than other anatomical sites. The review load was approximately constant over time.

Pretreatment QA in isolation can neglect inconsistencies such as those arising from possible machine, setup, and/or anatomical changes. Such inconsistencies can sometimes arise during the normal course of treatment, but all should be detected efficiently and analyzed with proper care. The role of IVV is to provide notification, via flags, when unexpected changes occur. Clinically, the impact and manipulation of flags still needs to be fully explored. One concept of particular interest is the notion of reconstructing the deposited dose in flagged cases to analyze cases that triggered action levels. Further efforts will seek to elucidate and solidify this potential.

We have now implemented a tool in TomoTherapy machines that performs adaptive dose recalculation. The program is completely automatic and gathers the information from the same archives as those used in in-vivo verification. The program extracts the daily MVCT creating a merged CT at the location where the patient was treated, taking into account the image registration used for treatment. A merged image is a CT that contains the complete MV CT that was imaged, with the planning kV CT completing the rest of the image. This merged CT is used to compute the fraction dose. The dose calculator is a convolution superposition[42-44] dose calculator. To be more efficient, our implementation is GPU based. A deformable registration algorithm based on morphons[45,46] was used to generate daily contours and analyze daily and cumulative DVHs. The deformable registration also provides deformation maps that allow mapping the daily doses back to the planning CT in order to compare the planned dose with the cumulative actual delivery. A GUI allows the user to analyze the registration, contours, and daily and cumulative doses. We have implemented adaptive dose recalculation on five linacs as well. As part of a future work, we will also evaluate the clinical relevance of the flags provided by in vivo verification based on portals.

Based on this large data set, it appears that the behavior per anatomical site for linacs and TomoTherapy it is very similar, even when daily CT guidance is used in the latter.

Finally, these data suggest that the implementation of an IVV program can validate consistency during treatment and flag for verification if an action level is violated. Additional studies will need to be performed to gauge clinical impact if an adaptive dose recalculation process is implemented. Though it will require increased resources and effort by the radiation team, such a program would allow for detection of issues during the treatment period itself.

4 - Conclusions

These data suggest that significant improvements in treatment consistency can be obtained and maintained by performing IVV on a daily basis.

IVV was successfully used to signal consistency errors in exit dosimetry in more than 6 million fractions among 84 clinics. This “big data” set eoncompasses the equipment of most external radiotherapy manufacturers (Varian, Siemens, Elekta and TomoTherapy).

Verification during treatment may detect issues that would otherwise go undetected. The number of verifications required during the course of treatment was anatomically dependent. For head and neck, breast, and lung, approximately 20% of the weekly verification portals triggered action levels. Such portals triggred action levels in 13% of pelvis and less than 10% of prostate cases. It should be noted that the level of flagging for each anatomical site was similar for linacs and TomoTherapy. In the linacs, flagging criteria of 3% 3mm and 5% 5mm were used, with either 2D portal or cone beam CT IGRT. For all TomoTherapy cases, 3% 3mm criteria and CT guided were used.

During the course of treatment, between one and two weekly portals per patient, on average, triggered actions levels requiring verification. Compared to the current standard of treatment of isolated pretreatment QA, this may imply an increased workload for the medical team in exchange for optimization and verification of procedures.

FIGURE 1

WORKFLOW DIAGRAM FOR THE IN-VIVO VERIFICATION TECHNIQUE USED.

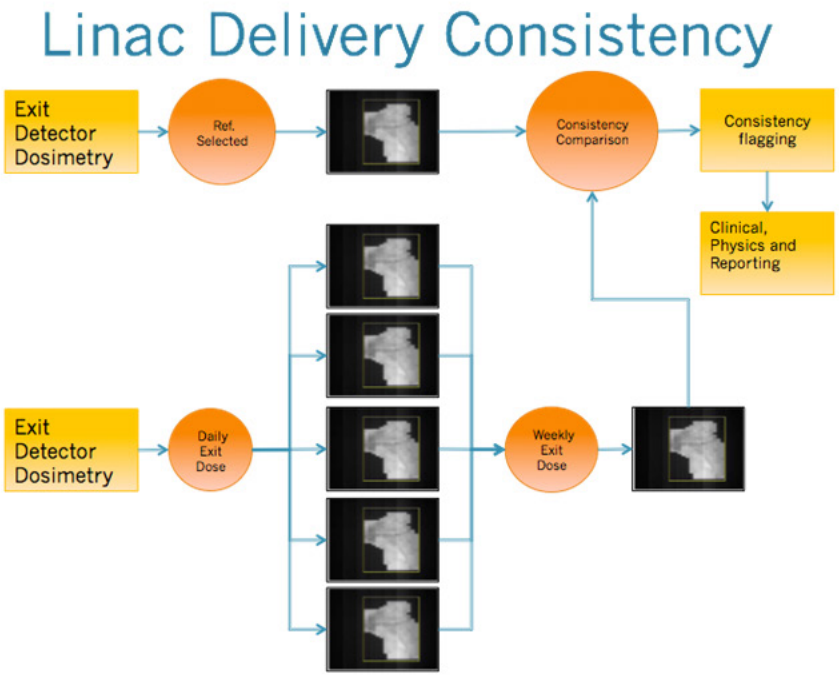


Figure 2

Table used during the troubleshooting procedure when action levels are flagged.

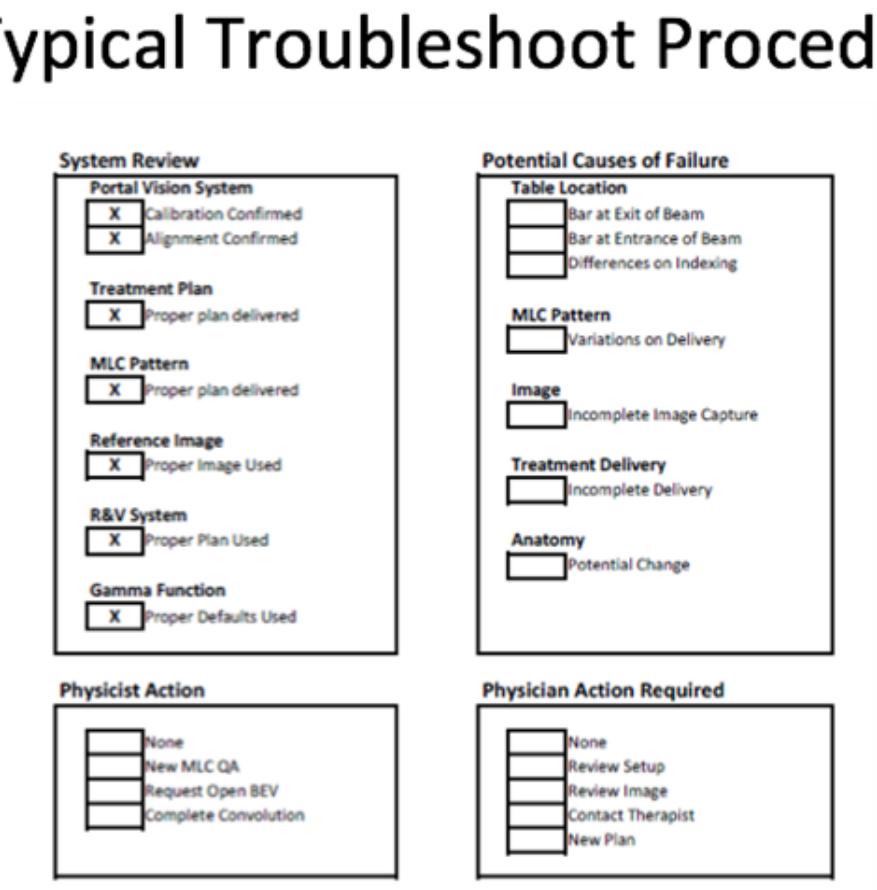


Figure 3

Description of the linac data sets available for analysis.

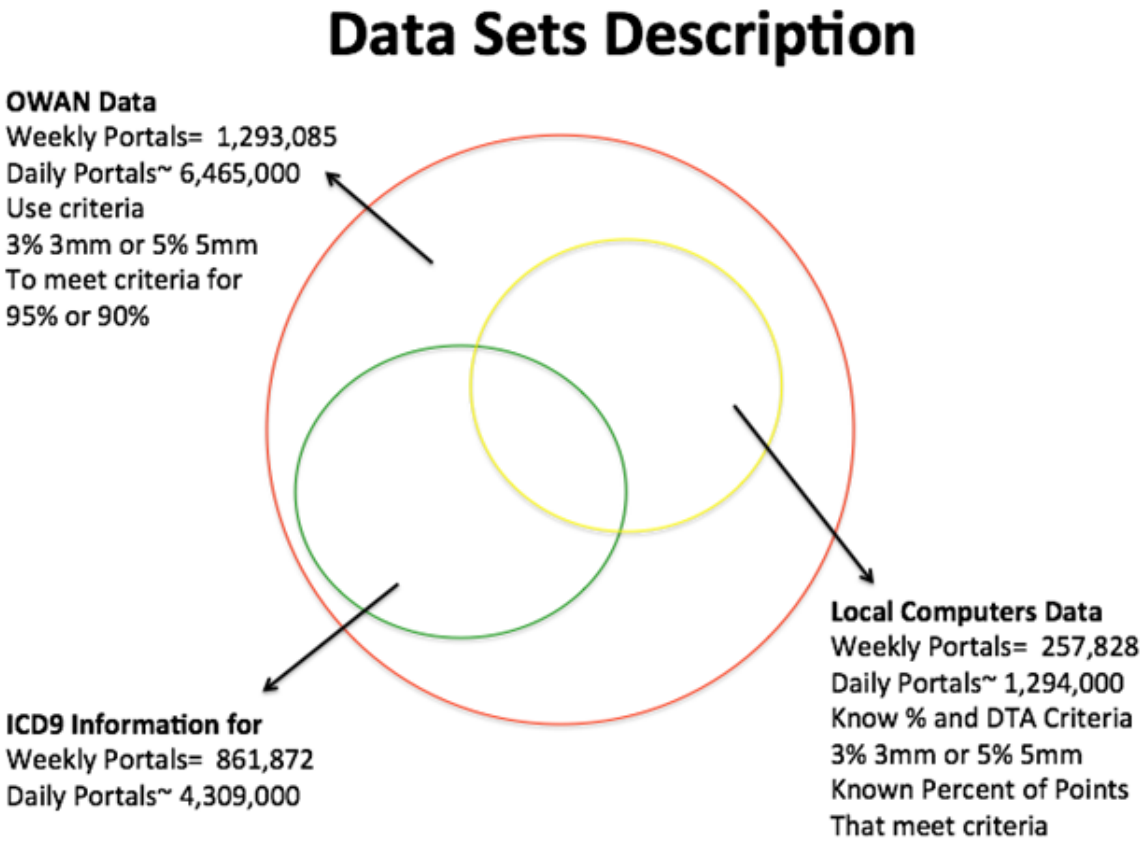
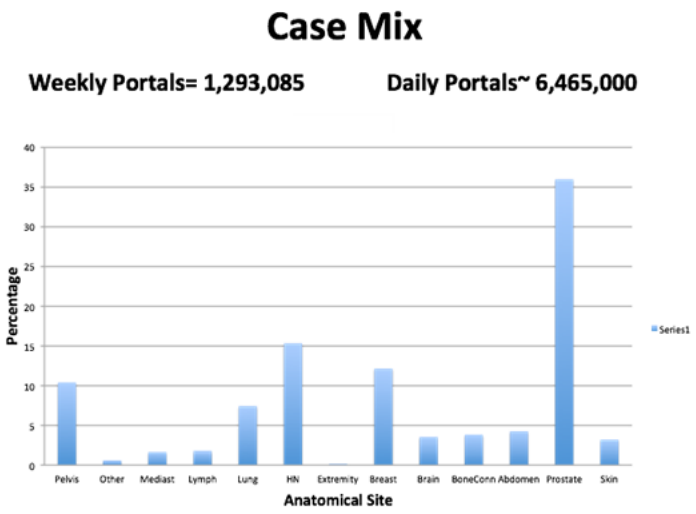


Figure 4

a) Description of the case mix used on this analysis. The cases were sorted using ICD9 information.



b) Histogram of percentage of passing points for weekly portals for the 3% 3 mm and 5% 5 mm criterias.

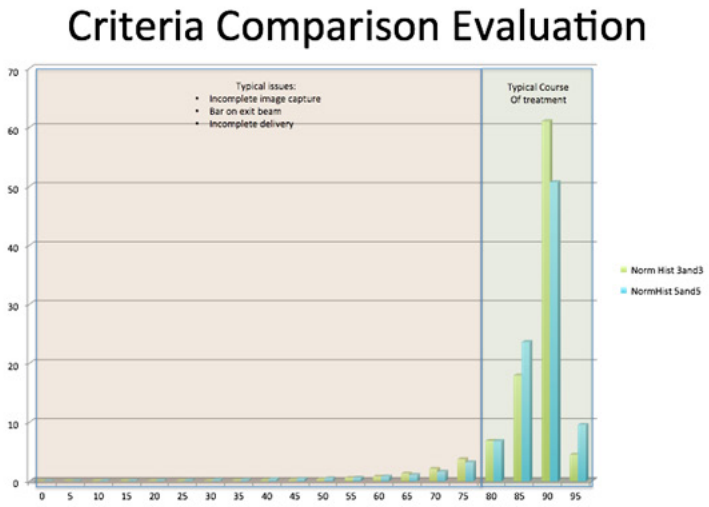
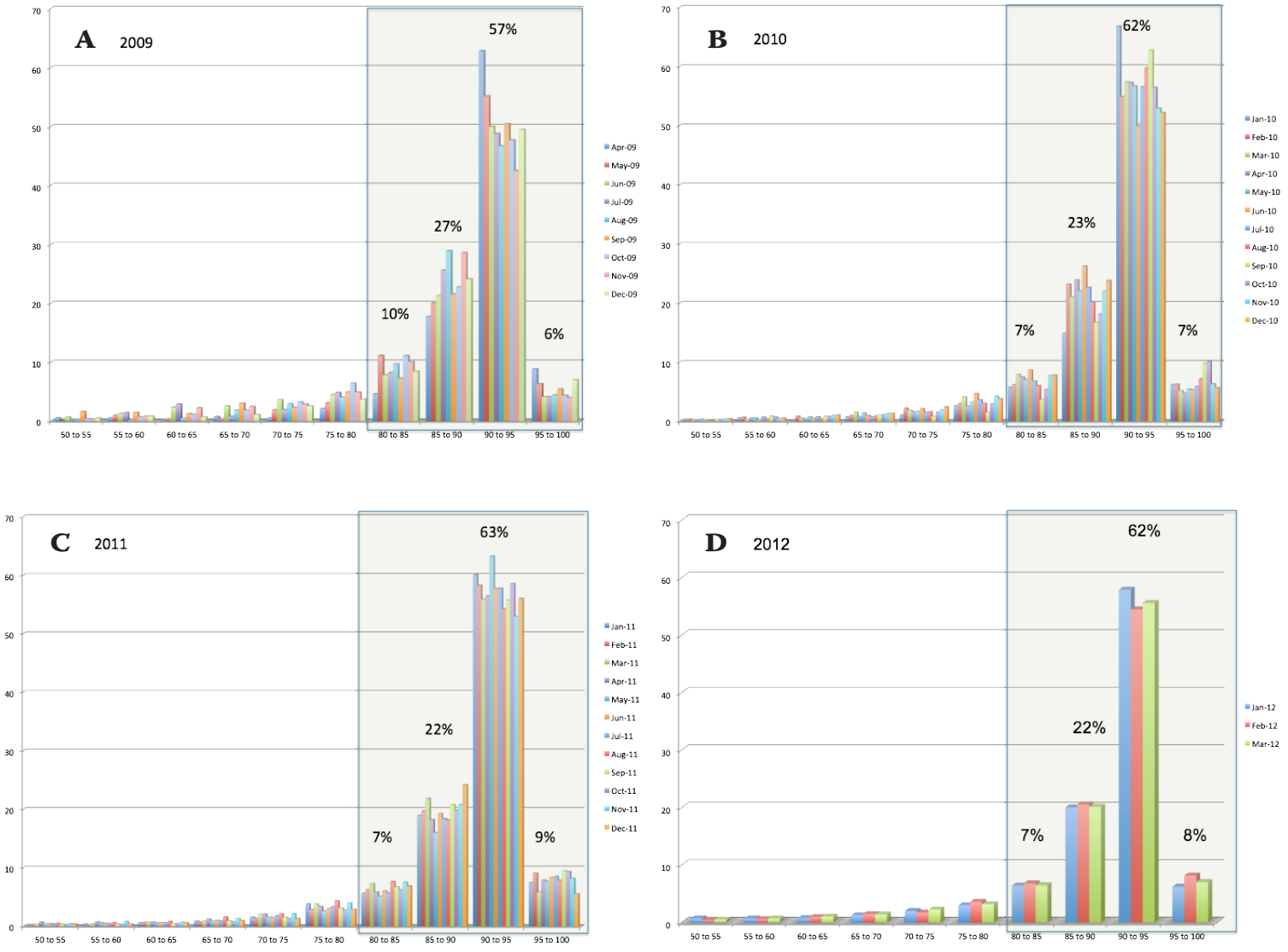


FIGURE 5

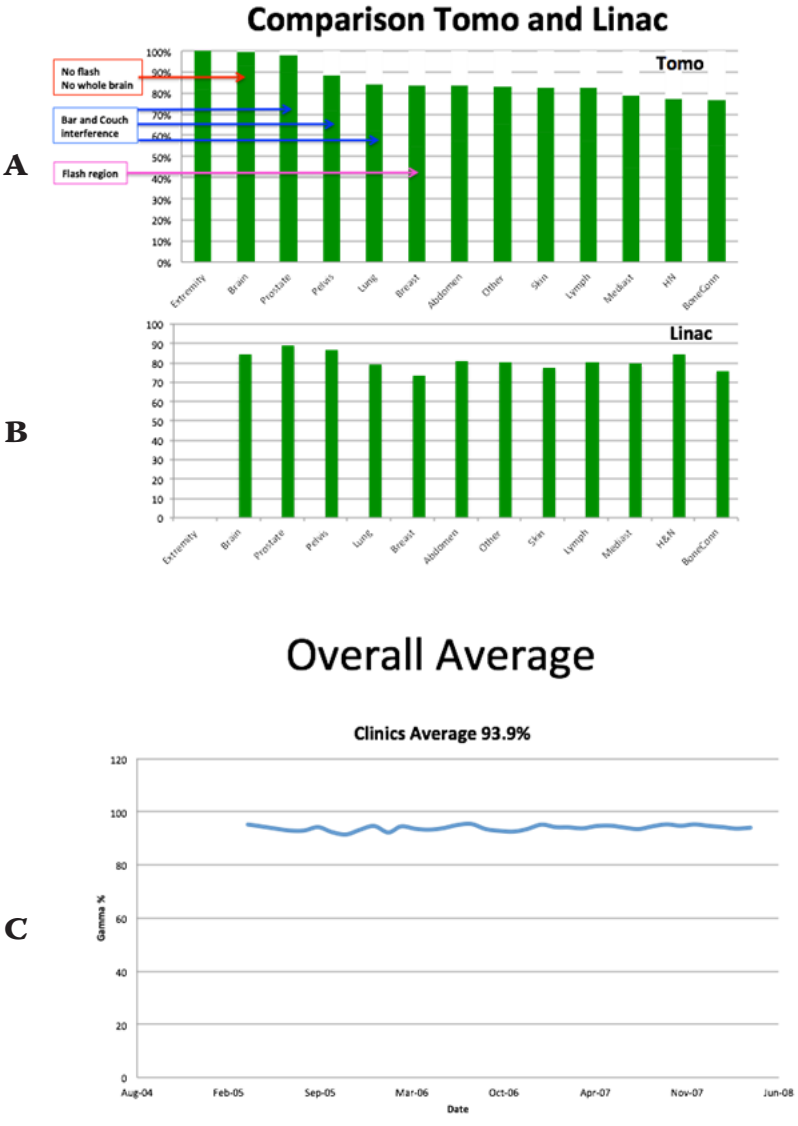
HISTOGRAM OF PERCENTAGE OF PASSING POINTS FOR WEEKLY PORTALS FOR EACH MONTH



A) 2009, B) 2010, C) 2011, D) 2012.

Figure 6

Percentage of weekly portals passing in-vivo verification criteria for different anatomical sites.



a) Linacs, b) TomoTherapy, c) Overall passing percentage as function of time

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