Critical Analysis of strength-based Medical Event Definition in prostate seed brachytherapy based on a comparative retrospective pre- and post-implant analysis.

This study is meant to create a clinical basis as well as to describe a process based upon one would be able to create a meaningful definition of ‘treatment site’, based on the knowledge accumulated so far on what a good implant is.

We studied 100 cases. Mean prostate volume for pre-plans was 32.3±11.9cc (range 12-61cc) while post-plans volume was 32.3±11.9cc (range 15.6-65cc), showing a consistent outlining of prostate on ultrasound and CT. Average D90 decreased from an average of 115.1±6.7% for pre-plans to 103.0±13.7% in post-plans. The number of seeds pre-planed ranged from 45 to 115 and an average of 3 seeds was added to preplans during implants.

A central element of the study was creating “zones” outside of pre- and post-plan contoured prostate structures and evaluating each case by the number of seeds ≥ 20% outside of a “zone” ranging from [0, 1, 2, 3, 4 and 5mm]. The result is shown in Fig. 1.

Based on the data we studied, defining a ‘treatment site’ as the inclusion zone of 4 mm outside of the commonly delineated CT prostate, would have produced no medical events based on the new definition. A 3mm zone would have triggered the rule for 5 cases, while a 2mm zone would have singled out 14 cases. Of course all implants studied were appropriate and had good coverage, as described by D90. A linear decrease of D90 was identified as a function of increasing zone, from an average of 100% in zone 0 to less than 89% in zone 4. This shows that D90 prostate coverage is in fact congruent with the “20% or more seeds outside” of a zone rule.

In order to study the similarity between a pre-plan and a post-implant plan, we calculated the skewness and kurtosis of the inter-seed distance distributions. Pre-plans had a mean skewness of 0.06 (compared with 0 for a normal distribution) while for post-plans the value was 0.14, showing a spread of inter-distances towards larger values. A “minimum box” concept was used to describe the extent of the seeds in an implant. The same spread captured by skewness was evidenced by the increase of the “minimum box” encompassing 100% and 95% of the seeds (this last one was used to deal with possible outliers). The ratios of the post- and pre-plan “box” increased from 1.4 in zone 0 to 1.72 in zone 3, showing the in the cases that still had 20% or more of their seeds placed outside of zone 3, the seed ‘cloud’ expanded significantly more than it was planned to. It is not possible to distinguish between edema and placement errors. Kurtosis, a measure of how much ‘oulier-prone’ a distribution is, revealed, as expected, a significant increase in the post-plans, but no correlation with the cases having more than 20% of the seeds in distant zones.

Comparing pre- and post-plans one can see (Figure 1) that there is no correlation between pre-plans and post-plan zones. If a pre-plan was created with more than 20% of the seeds in zone 2 (e.g patient 54), the post-plan would not necessarily reflect that.

Another measure we studied was the shift between the center of mass of the prostate contours and the center of mass of the seed distribution. In all zones, the shift increased from 1.87±0.93 in pre-plans to 3.57±1.43 in post-plans. While the average shift did not vary with the zone index, the minimum values did, from 0.5mm in zone 0 to 5.2mm in zone 3. It is also interesting to note that the mean seed distances (measured from the CM of the implant) decreased from
19.1±2.1mm from pre-plans to 17.7±2.1mm in post-plans, while the seed ‘boxes’ increased, showing more ‘scattered’ distributions.

![Figure 1. Percentage of total number of seeds found at distances 0-5mm from Prostate. Each of the 100 patient plans (pre-left and post-right) is a horizontal band and the color reflects the percentage of the total number of seeds outside of a certain zone defined by the distance from Prostate. The deep blue ‘background’ shows a percentage of seeds less than 20%.](image)

We believe that this is a very timely study at a moment when the Radiation Oncology community searches for better, more reliable ways not only to define medical events but in general to quantify pre- and post-implant similarity. We have developed tools and a process that will allow users to better define and assess, based on their own clinical data, the quality of prostate permanent seed implants.