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Original paper

Impact of spot size variations on dose in scanned proton beam therapy

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ABSTRACT

Background: In scanned proton beam therapy systematic deviations in spot size at iso-center can occur as a result of changes in the beam-line optics. There is currently no general guideline of the spot size accuracy required clinically. In this work we quantify treatment plan robustness to systematic spot size variations as a function of spot size and spot spacing, and we suggest guidelines for tolerance levels for spot size variations.
Methods: Through perturbation of spot size in treatment plans for 7 patients and a phantom, we evaluated the dose impact of systematic spot size variations of 5% up to 50%. We investigated the dependence on nominal spot size by studying scenarios with small, medium and large spot sizes for various inter-spot spacings. To come to tolerance levels, we used the Γ passing rate and dose-volume-histograms.
Results: Limits on spot size accuracy were extracted for 8 sites, 3 different spot sizes and 3 different inter-spot spacings. While the allowable spot size variation strongly depends on the spot size, the inter-spot spacing turned out to be only of limited influence.
Conclusions: Plan robustness to spot size variations strongly depend on spot size, with small spot plans being much more robust than larger spots plans. Inter-spot spacing did not influence plan robustness. Combining our results with existing literature, we propose limits of ± 25%, ± 20% and ± 10% of the spot width σ, for spots with σ of 2.5, 5.0 and 10 mm in proton therapy spot scanning facilities, respectively.

1. Introduction

In Intensity Modulated Proton Therapy (IMPT), dose is delivered to the patient by combining the dose from numerous small proton beams (spots) with a certain lateral size, energy, position, and number of protons. To ensure that the planned and delivered dose correspond, the spot characteristics must be stable. The lateral size of the spots is a parameter for which it is challenging to guarantee perfect stability over time [1–5]. Beam size changes could occur as a result of variations in the proton accelerator (e.g. beam energy, divergence, offset) and in the beam transport (magnet currents, gantry). If beam size modifications persist over many fractions, dose modifications in the patient can occur, with the risk of compromised target coverage and/or overdosage in critical structures [1–4].

Although the importance of spot size stability is known, literature is scarse and there are no general guidelines available on recommended values of this parameter for existing and future proton therapy spot scanning facilities. Chanrion et al.[1] report that dose modifications can occur for beam size changes ⩽25%, based on dose parameters for prostate and skull-base patients. Parodi et al. [3] suggest ± 50% as tolerance limit, based on target coverage for a spherical phantom. Finally Lin et al. [4] report ± 10%, based on the Γ analysis of 28 patients.

None of these studies systematically studied the dependence on beam width and inter-spot distance, and moreover none of these studies reported both dose parameters and the Γ analysis together. The latter is useful to understand the full impact of spot size inaccuracies, both in view of machine commissioning as well as patient safety.

The goal of this work is twofold. First, we intend to quantify the clinical influence of spot size changes as a function of spot size and inter-spot distance. This will be done by performing a robustness analysis for 7 patients and a phantom. Second, we combine our results with the existing literature to extract tolerance levels for spot size changes.

2. Methods and materials

Our patient group (Table 1) consists of 7 patients (pelvis, chest-wall, rectum, chordoma, cardiac, retro-peritoneal, spinal sarcoma) and 1 phantom. For each case we created treatment plans with the Astroid treatment planning system [7,7]. For optimizing the target and organ-at-risk dose, multi-criteria optimization is used, based on the computation of a set of Pareto optimal plans [8]. Plans were made with 3

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Table 1
Summary of the 7 patients and the water phantom: site, target names, target volumes, prescribed dose D_T, number of fractions N_{fx}, prescribed dose per fraction D_{Rx}, number of fields N_F, and usage of range shifters (RS). CTV and CTVHR are Clinical Target Volume and Clinical Target Volume High Risk, respectively, where the latter is the part inside the CTV receiving a boost dose.

Site	Target name	Target volume [cc]	D_T Gy(RBE)	N_{fx}	D_{Rx} Gy(RBE)	N_F	RS (cm)
Pelvis	CTV	1020	45	30	1.5	2	8
Chest Wall	CTVHR	1019	50	25	2.0	1	8
	CTV	1091	45		1.8		
Rectum	CTVHR	217	50	28	1.8	2	4
	CTV	787	45		1.6		
Chordoma	CTV	14	72	36	2.0	4	0
Cardiac	CTVHR	57	50	25	2.0	2	8
	CTV	435	45		1.8		
Retro-peritoneal	CTVHR	1024	38	17	2.2	1	8
	CTV	3,198	31		1.8		
Spinal sarcoma	CTV	464	18	10	1.8	2	8
Phantom	CTV	1000	30	15	2.0	1	0

different spot widths (values at iso-center in air): small spots ($\sigma = 2.5$ mm at 230 MeV to $\sigma = 5$ mm at 69 MeV), medium spots ($\sigma = 5.0$ mm at 230 MeV to $\sigma = 10$ at 69 MeV), and large spots ($\sigma = 10$ mm at 230 MeV to 20 cm at 69 MeV). For each spot size we created plans with 3 lateral inter-spot distances (in air): 1 σ, 1.5 σ, and 1.75 σ. The longitudinal layer spacing was 0.8 times the distal Bragg peak width. In all plans we aimed at $V95\% > 98\%$ and $V107\% < 5\%$, but more flexibility was allowed for the spinal sarcoma and cardiac patient to better spare the organs-at-risk, in accordance with clinical guidelines. The plans were all clinically validated. For the chest-wall patient, the optimizer could not find a solution for large spots with $d = 1.75\sigma$. The total number of nominal dose distributions D_{nom} was 71 nominal dose distributions 71 (8 cases × 3 beam widths × 3 inter-spot distances − 1 infeasible plan = 71).

To evaluate the effect of a systematic change in spot width, we created perturbed dose distributions D_{mod} by re-calculating in the Astroid scripting environment all the nominal plans with modified spot widths without re-optimizing. For each spot size, we simulated variations in spot size at iso-center in air of ± 5%, ± 10%, ± 15%, ± 25%, ± 35% and ± 50%. In total, the number of modified dose distributions was 852: 71 nominal dose distributions ×12 spot size variations = 852.

2.1. Analysis

We analyzed the impact of spot size variations on dose by comparing the perturbed dose matrix D_{mod} against the nominal dose matrix D_{nom}. We analyzed the following dose metrics.

- Pass Rate Γ. We evaluated the pass rate Γ for the γ function [12,12] in 3D, with tolerances of 2 mm and 2% of prescribed dose, threshold 10% of prescribed dose, and $\Gamma > 90\%$ acceptable, in accordance with the AAPM Task Group Report 119 [13]. We used a previously in-house developed C++ code for calculating the γ function [12].
- Dose-volume histograms (DVH) histograms and associated parameters like V95% and V107%. We used the C++ based analysis framework ROOT to extract them.

3. Results

In Fig. 1 we display Γ as a function of the spot size deviation for our 8 cases for medium spots and inter-spot spacings of 1σ, 1.5σ and 1.75σ. Results for small and large spots are given in the Supplemental Material. By comparing the black, green and black lines in Fig. 1, we notice that the inter-spot distance had generally only a very small impact on the impact of spot size deviations (see Section 4).

For each patient, we indicate at which spot size deviation the Γ crosses the 90% value, taking an inter-spot distance of 1.5σ as reference [9,10]. The extracted limits based on the criterion $\Gamma > 0.9$ are given for all patients in Table 2 for an inter-spot distance of 1.5σ. The overall limit, which is the most strict limit found for all cases, is given as well. We note from Table 2 that small spot plans are more robust to spot size changes than large spot plans when considering relative errors.

In Fig. 2 and Fig. 3 we display the V95% and the V107% as a function of spot size deviation for medium size spots, respectively. In the Supplemental Material we give the corresponding figures for small and large spots. These figures confirm that inter-spot spacing has not much influence on dose, and that small spot plans are more robust than large spot plans.

From Figs. 2 and 3 we observe moreover that changes inthe V95% and the V107% can be dramatic, even though the Γ passing rate is sufficiently large. This is seen for instance for the chordoma case: for medium size spots the maximum allowed deviation is +27% following the Γ analysis, however this would result in dramatic V95% of only about 75%. And a deviation of −44%, the maximum tolerance level following the Gamma analysis in the Water phantom, would result in a V107% that is higher than 50%. A similar though less dramatic situation occurs for other patients. In the chordoma case, we believe the small size of the target, the strongly modulated dose, and the large number of beam directions make it a complicated case. We come back to this in Section 4.

It is illustrative to understand where the dose differences, defined as modified dose minus default dose, were generally located. Fig. 4 gives an example of the dose effect of a −35% and +35% beam size change on the dose for the pelvis patient for medium size spots, for 4 dose slices. We note that:

- For a beam size decrease (Fig. 4i-l), an overdose (positive dose difference) occurs at the target borders that are parallel with the incoming beams and at beam entrance, while inside the target the dose is more or less unchanged. The overdose at the borders of the target explains the increase in V107% with decreasing beamsize that was seen in Fig. 3a.
- For a beam size increase (Fig. 4m-p), we note that an underdose occurs at the borders of the target, while inside the target dose differences are very small. In other words, dose 'leaks out' in all directions. This explains the decrease in V95% with increasing beamsize that we saw in Fig. 2a.

The above observations are roughly true for all patients and all beamsizes.

4. Discussion

The above study demonstrated the possible clinical impact of spot

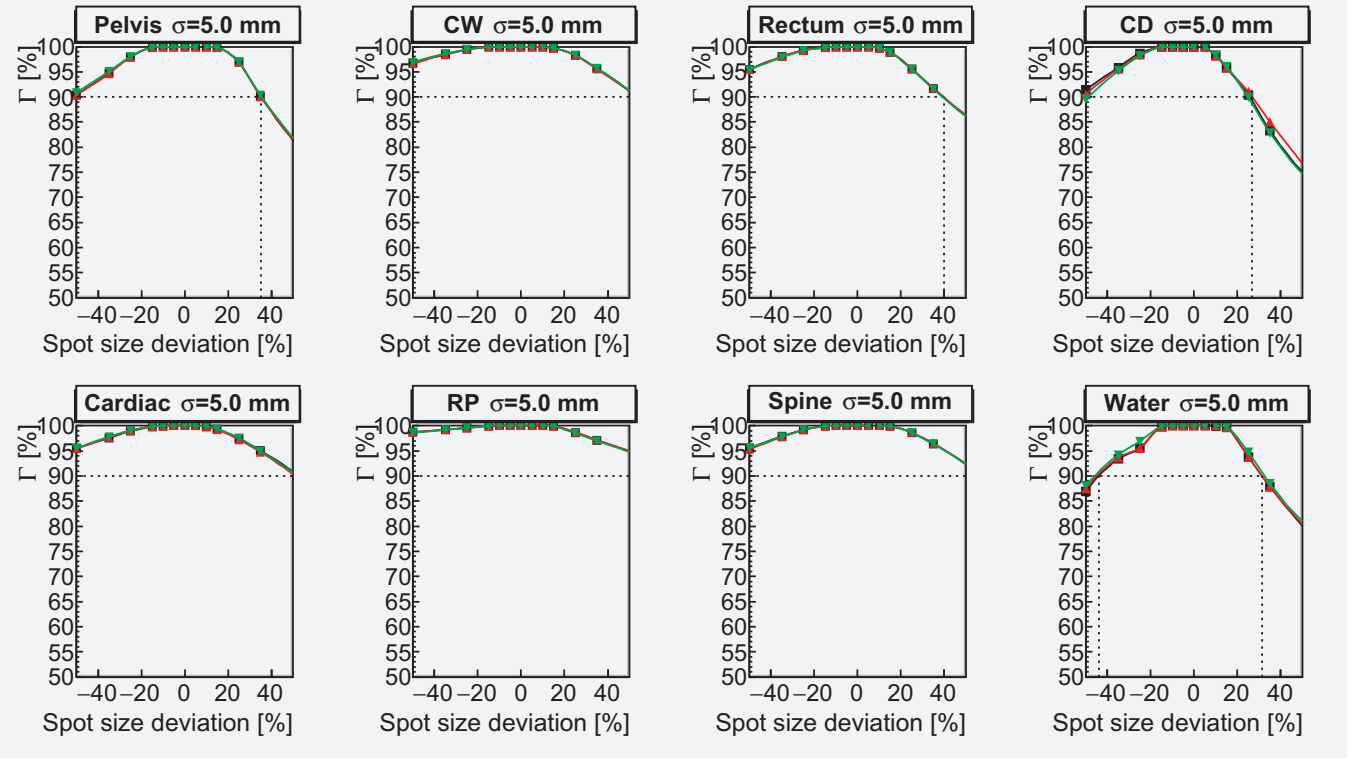

Fig. 1. Gamma passing rates (Gamma tolerance (2%, 2 mm), dose threshold 10% of prescribed dose) for various patients of the spot-size perturbed plans, for medium size spots. The three curves represent the different inter-spot distances: $d = 1\sigma$ (black, invisible since it's covered by the red and green line), $d = 1.5\sigma$ (red) and $d = 1.75\sigma$ (green). The dashed lines indicate how the tolerance levels were determined (black dashed line) through interpolation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Largest allowed spot size deviation (in %) that assures $\Gamma > 0.9$ for small, medium and large spots for our patient cohort, for an inter-spot distance of 1.5σ.

Site	Small spots		Medium spots		Large spots	
	Negative	Positive	Negative	Positive	Negative	Positive
Pelvis	<-50	>50	<-50	35	−18	13
Chest-Wall	<-50	>50	<-50	>50	−32	23
Rectum	<-50	>50	<-50	40	−30	16
Chordoma	<-50	44	<-50	27	−37	18
Cardiac	<-50	>50	<-50	>50	−34	23
Retro-peritoneal	<-50	>50	<-50	>50	<-50	39
Spinal sarcoma	<-50	>50	<-50	>50	−34	25
Water Phantom	<-50	>50	−44	31	−13	12
Overall limit	<-50	44	−44	27	−13	12

size inaccuracies for different beam widths and different inter-spot distances for a new patient group. Our study has revealed several new issues and complements previous work about spot size variations.

This work is the first study where the impact of spot size and inter-spot distance on plan robustness to spot size changes has been studied in a systematic way. We found that spot size has a strong influence on the dose impact and associated tolerance limits: small spot plans are much more robust against spot size changes than large size spots (Table 2). This is mostly due to the fact that we evaluated relative changes in spot size. When considering a certain relative error size, plans with large spots are significantly more perturbed on an absolute scale than plans with small spots. We chose to report relative values to be in accordance with previously published work in this context [1–4].

Concerning lateral inter-spot distance, we notice from Figs. 1–3 that inter-spot distance does not significantly affect the Gamma analysis nor the DVH parameters. We believe that in-patient scatter blurs the effect of the inter-spot distance.

We noticed that the DVH parameters and the Gamma passing rate can lead to different conclusions with regard to acceptability of the perturbed dose distribution. Similar issues have been reported earlier in the context of IMRT [14,15]. We believe the following factors are important:

- Dose normalization. If many points on the dose matrix have a nominal dose that is already near 107% of the prescribed dose, this can result in a easily perturbed V107%. The same is true for the V95%. For the Chordoma patient, we verified that the V107% was more robust when the dose was slightly scaled down, however the V95% was somewhat less robust.
- Threshold in Gamma passing rate. The calculation of the Gamma passing rate considers a much larger region around the target than the V107% and V95% parameters, because the dose threshold was 10% of prescribed dose (Section 2.1). In other words, the γ analysis and the target coverage parameters consider partly different dose regions. Increasing the dose threshold in the calculation of the Gamma passing rate from 10% to 80% leads to somewhat more stringent results, as can be seen from Fig. 5. The threshold of 10% used in Table 2 is most commonly used, so we consider that as standard.
- Other free parameters in the calculation of the Gamma passing rate: dose/distance criteria. More stringent parameters lead to more stringent limits, and vice versa. The 2 mm/2% criterium we report is commonly used.
- Other parameters that influence dose penumbra, like target shape and number of beam directions (see below).

The values in Table 2 and Figs. 2 and 3 can be compared with results from existing literature [1,3,4]. Using small spots Chanrion [1] reported that changes of ± 10% did not pose any clinical hazards, and changes of

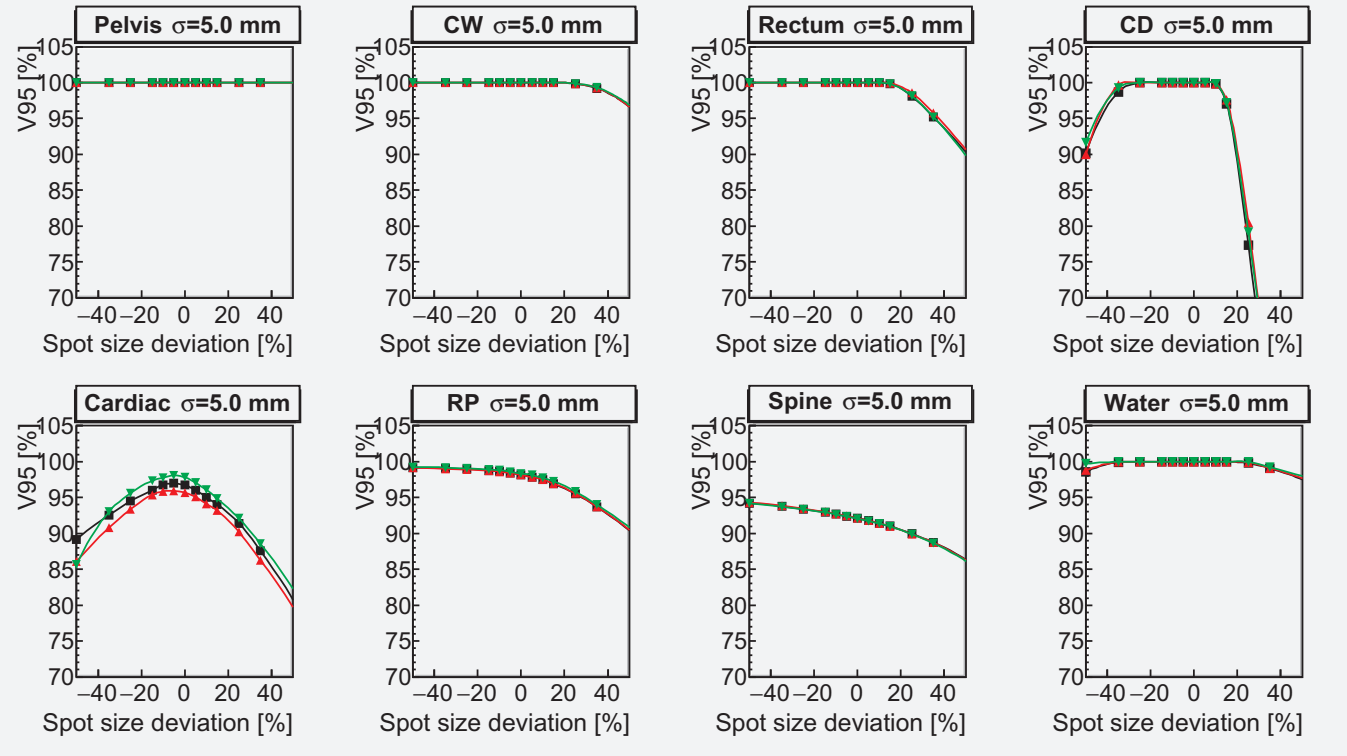

Fig. 2. V95% for various patients as a function of the spot-size deviation, for medium size spots. The three curves represent the different inter-spot distances: $d = 1\sigma$ (black), $d = 1.5\sigma$ (red) and $d = 1.75\sigma$ (green). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

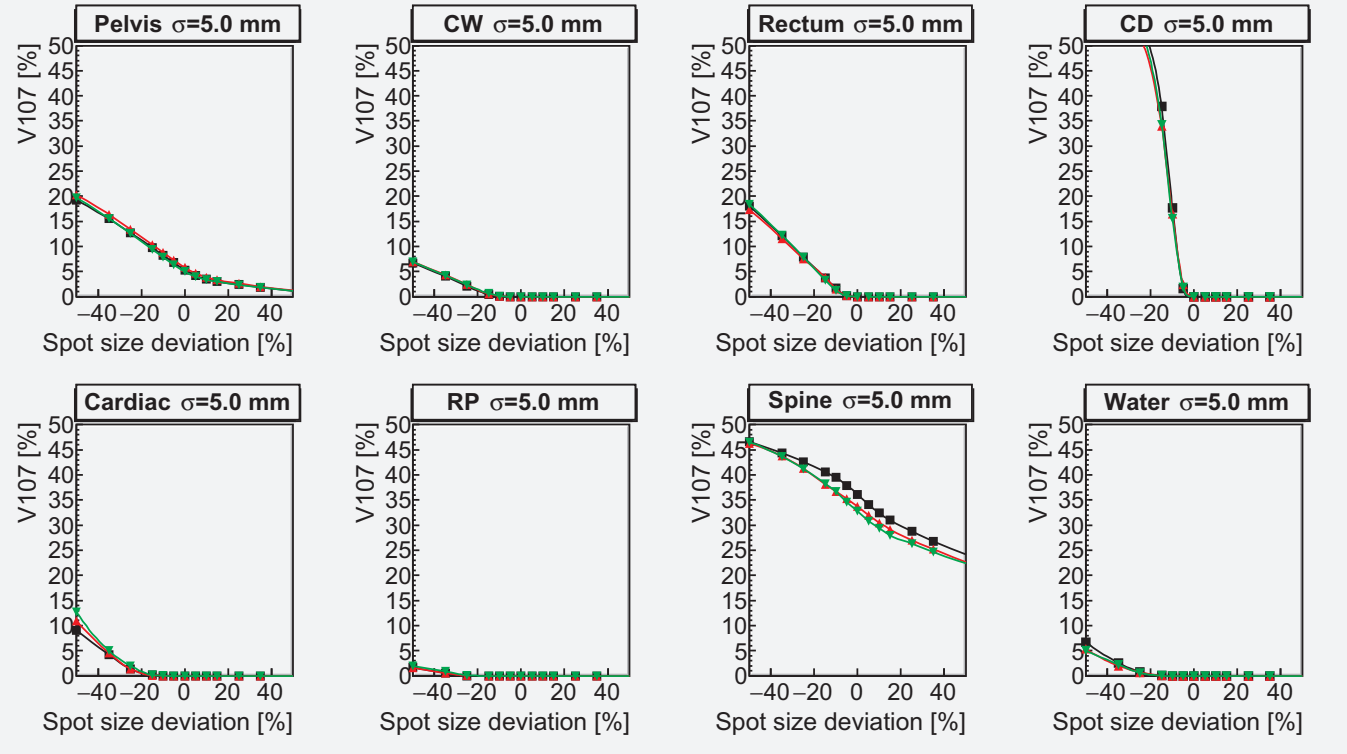

Fig. 3. V107% for various patients as a function of the spot-size deviation, for medium size spots. The three curves represent the different inter-spot distances: $d = 1\sigma$ (black), $d = 1.5\sigma$ (red) and $d = 1.75\sigma$ (green). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

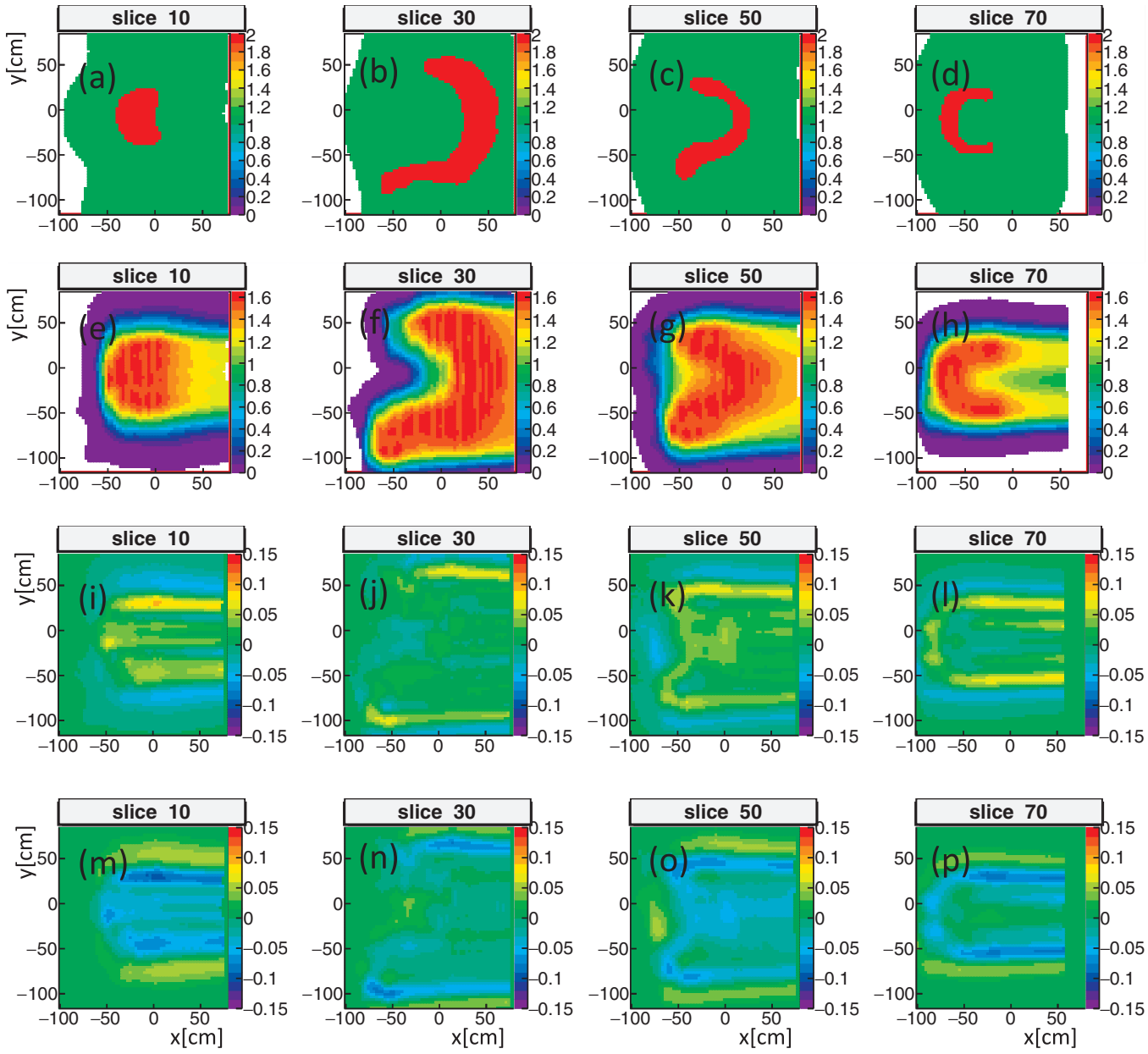

Fig. 4. Different slices representing the target structures (a-d) and default dose (e-h) for the pelvis patient, and dose difference between perturbed and default dose, for a −35% error (i-l) and a + 35% error (m-p). The x- and y-axis are in mm. The color-wash for figs. (a) to (d) indicate the target (red), patient (green) or outside patient (white). The color-wash in (e) to (p) represent fractional dose values in Gy (RBE). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

± 25% resulted only in some cases in dose degradations, both based on DVH parameters. This is well comparable with our results for DVH parameters, and stricter than our results of the Gamma analysis. For medium size spots (~ 5 mm), Parodi [3] suggested to trigger an interlock when beam size changes exceed ± 50%, based on a circular phantom geometry. The values we found are stricter. We suspect that the circular phantom geometry considered in [3] is relatively simple, and may not fully cover the problematics that could be encountered for real patients. For large spot sizes limits of ± 10% were reported by Lin et al. [4] based on the Gamma analysis, which are close to our limits for large spots given in Table 2.

There are a few limitations to the current study. First, we have chosen to study plan robustness as function of spot size and inter-spot spacing for a widely varying group of patients with different patologies and plans. The disadvantage of this is that it is difficult to understand the influence of specific parameters, like target volume, target shape, number of fields, range shifters, target depth, margins, and so on. These can all influence plan robustness. Although systematic studies of these issues are part of future research, a few remarks can be made. For instance, penumbra size is affected by the shape of the target: in circular/compact targets, less dose is lost in penumbra than in lobular/irregular tumors. This could influence the response of the Gamma analysis. Target depth and usage of range shifters can influence plan robustness: more material implies more scattering, that could blur the dose effects. Regarding margins, they could influence plan robustness [16]. Dedicated studies for each patient would be needed to confirm this. Regarding the number of fields, on one hand a larger number of fields could reduce the risk of local hot and cold spots. On the other hand, issues such as dose leakage out of the target would remain equally problematic. Summarizing, there are many parameters that can

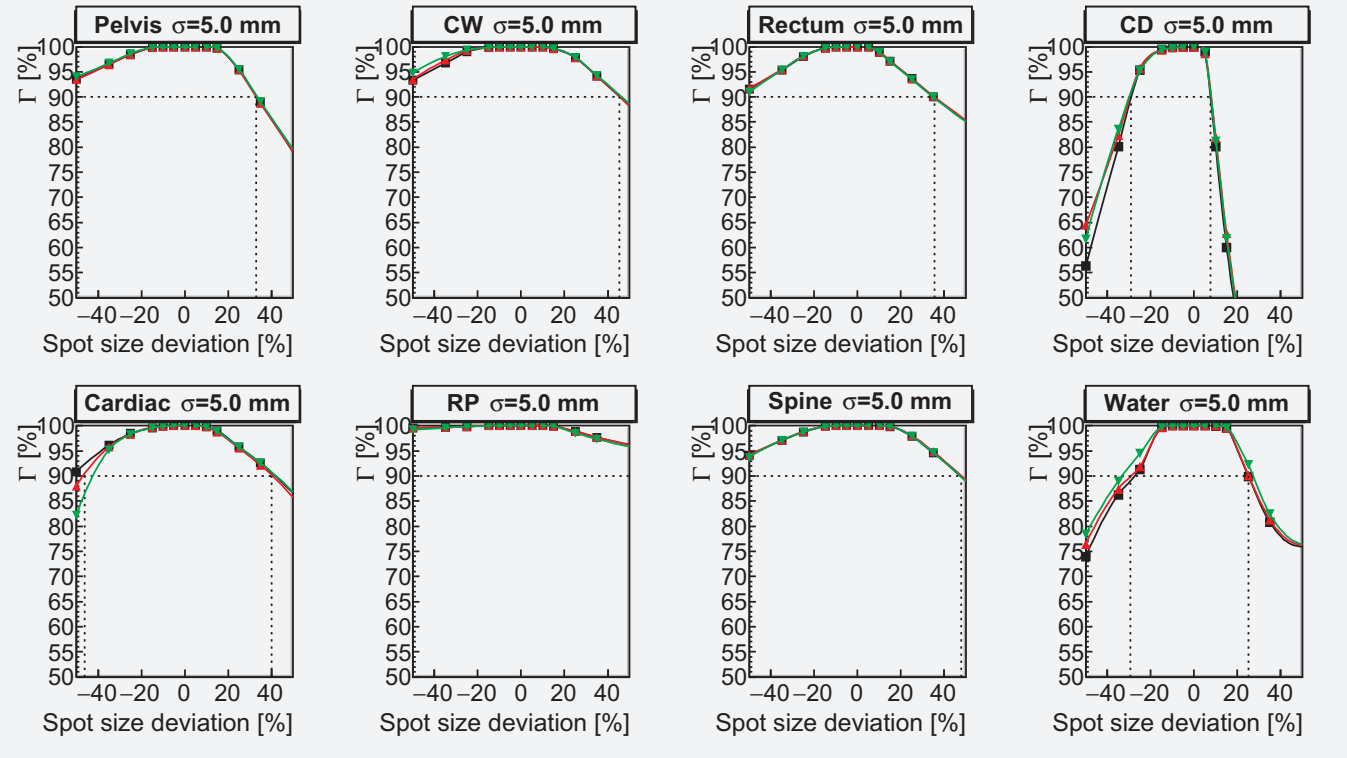

Fig. 5. Gamma passing rates (Gamma tolerance (2%, 2 mm), dose threshold 80% of prescribed dose) for various patients of the spot-size perturbed plans, for medium size spots. The three curves represent the different inter-spot distances: $d = 1\sigma$ (black, invisible since it's covered by the red and green line), $d = 1.5\sigma$ (red) and $d = 1.75\sigma$ (green). The dashed lines indicate how the tolerance levels were determined (black dashed line) through interpolation. Note that the limits are more stringent now than in Fig. 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

influence plan robustness to spot size changes. The advantage of our choice to study a variety of patient cases is that this allows us to obtain widely applicable tolerance levels.

Another limitation of the current study is the fact that we have not explicitly assessed the difference between SFUD and IMPT in our plans with more fields. Our plans were all IMPT plans. We believe that IMPT plans are more sensitive to beam size changes than SFUD plans. In SFUD, the dose is a result of a sum of an array of Gaussian spots, and is expected to remain fairly constant with variations in the width of those Guassians. In IMPT localized dose heterogeneities are expected to fit together to add to a prescribed dose, and thus spot size variations are expected to have a stronger impact on the delivered dose. A systematic study to the difference between IMPT and SFUD would have to confirm this.

For existing and future proton therapy facilities it is useful to have general guidelines for beam width variations. Based on (i) the Gamma analyses of the current study, (ii) the DVH parameter study of the current study, (iii) the work by Chanrion et al. [1], (iv) the work by Parodi et al. [3], and (v) the work by Lin et al. [4], we propose the following rough guidelines:

- -25% to 25% for spots with $\sigma \sim 2.5$ mm: very roughly the average between the result from our Gamma analysis ($< -50\%$ and $+43\%$) and the result reported by Chanrion et al. [1] for these beam sizes ($\pm 10\%$).
- -20% to 20% for spots with $\sigma \sim 5$ mm, which is roughly in between the results for 2.5 and 10 mm beams (next bullet), rounded upwards to a multiple of 5%.
- -10% to 10% for spots with $\sigma \sim 10$ mm, from the Gamma analysis in this study and that presented in Lin et al. [4].

Here σ is the spot width value at 230 MeV in air at iso-center. Beam size variations that persist over time should under all circumstances be kept below the above values. We stress that these values should be used only as *rough guidelines*, for instance in planning and constructing new facilities and in research aiming at developing new beam delivery systems. We strongly recommend that individual facilities ensure that (i) their beam width is constant in time, (ii) the exact values at which interlock systems react are carefully studied during clinical commissioning using the treatment planning system and strategies adopted by that facility, and (iii) that their treatment plans are robust to the size of beam size changes that can realistically be expected. The latter can be done for instance using in-house tools to perform robustness analyses, or by including beam size variations into the optimization process in the treatment planning system.

5. Conclusion

The impact of spot size variations is patient and spot width dependent. Small spot plans are much more robust to spot size changes than large spot plans. Inter-spot distance did not play a major role in the robustness of plans to spot size changes. As rough relative tolerance levels for proton beam width changes, we propose $\pm 25\%$, $\pm 20\%$ and $\pm 10\%$ for spots with $\sigma \sim 2.5$, 5, and 10 mm, respectively. Such rough guidelines can be used for instance during development, planning and construction of new proton delivery systems. We strongly recommend that individual proton therapy facilities ensure during clinical commissioning that their plans are robust against the size of beam size changes that can occur in their delivery system.

Disclosure of conflicts of interest

The authors have no conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, athttps://doi.org/10.1016/j.ejmp.2018.12.011.

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