Master of Science Thesis

Patient positioning correction strategies in radiotherapy:
A portal imaging study

By
Sofie Månsson

Supervisors: Håkan Nyström and Marika Lööf

Department of Medical Radiation Physics
The Jubileum Institute

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Abstract

Purpose: To find the optimal correction strategy to decrease the set-up errors for pelvic patients at the Department of Radiation Physics at the Finsen Centre, Copenhagen University Hospital.

Materials and methods: Using electronic portal imaging devise (EPID), 765 portal images from 17 patients, treated for bladder-, rectum-, anus- or gynecologic-carcinoma were aquired. The patients had the same set-up procedure. By comparing the DRR with the current portal image each patient's set-up deviation was determined. Once the statistical characteristics of the deviations were known, a set-up correction strategy could be applied. A computer program simulated set-up deviations for 1000 "patients" to find the optimal set-up corrections strategy.

Results: The standard deviation of the systematic set-up errors**,** $\Sigma_{set\text{-}up}$, was found to be approximately equal to the standard deviation of the random set-up error, $\sigma_{set\text{-}up}$ for the investigated pelvic patients. There was no significant overall mean systematic error. The computer-simulated study showed that the optimal correction strategy was the No Action Level (NAL) strategy with 3 measurements, with the Adaptive Maximum Likelihood (AML) factor included. Applying this strategy to the measured clinical data, the standard deviation of the systematic set-up error**,** $\Sigma_{set\text{-}up}$, decreased between 54 % and 71 %.

Conclusion: The suggested correction strategy resulted in potentially improved set-up accuracy with a relatively small increase in workload.

1. Introduction

This work has been performed as a thesis for the degree of Master of Science in Medical Physics at the University of Lund. It has been carried out at the Department of Radiation Physics at the Finsen Centre, Copenhagen University Hospital.

The ambition of radiotherapy is to kill tumour cells within the clinical target volume (CTV). The Planning Target Volume (PTV) contains of a CTV plus a margin that takes geometric uncertainties into consideration, see Appendix.
Too large a margin gives unnecessary dose to surrounding organs at risk, but too small a margin will result in an increased probability for geometrical misses at some or even all treatment fractions. A treatment uncertainty can be an uncertainty in organ shape and motion, beam geometry and patient set-up [6].
The patients´ set-up displacement, μ, corresponds to the difference between a reference image (DRR) and the portal image. It is assumed that μ is the sum of the systematic and random contributions. To prevent a discrepancy in the set-up, it is important to define the statistical characteristics of the deviation before any correction is made, and then reduce the systematic part [4]. If a random deviation is corrected for, it may introduce a new systematic deviation.
If there is the possibility to measure and, if needed, correct for the displacement on-line before irradiation at every fraction during the course of treatment, than there is no need to analyse the relation between the systematic and the random part, because then the set-up is optimised at each fraction. But, since this method cannot generally be performed automatically, workload considerations prevent this method from being used in practice.
Set-up deviations have been divided into systematic and random contributions by analysing the measured displacement μ in a series of portal images. The systematic contributions are due to differences in the patient set-up at preparation and the actual treatment, and the random contributions are due to day-to-day variations in the patient set-up during the course of treatment [17].
A systematic set-up deviation can be estimated from the overall mean of a number of set-up deviations of a particular patient [9]. This individual systematic set-up deviation m_p can differ from patient to patient, due to an arbitrary component in the transfer of data from simulator to

treatment machine. The individual random component due to daily set-up variations is determined by the distribution of set-up deviations around this mean m_p [3].

To be able to find the optimal correction strategy for a specific group of patients, it is necessary to determine the group's systematic set-up error $\Sigma_{set\text{-}up}$, which is defined as the standard deviation of the distribution of all patient's individual systematic set-up deviation m_p. The group's random set-up error $\sigma_{set\text{-}up}$ is defined as the standard deviation of the distribution of all patient's individual random set-up error [9].

Once the relation between the systematic and random errors is known, an appropriate correction strategy can be applied.

Presently at the department a portal image is taken during the first fraction. If there is a deviation μ of more than 5 mm compared to the reference image, the deviation is corrected by the total error $-\mu$. No further set-up measurements are performed during the rest of the treatment.

The theory behind this routine is that if the deviation is small it is believed to be either an individual random set-up deviation and, hence should not be corrected for, or a small insignificant individual systematic set-up deviation.

If the set-up deviation is large, it is believed to be an individual systematic one, which needs to be corrected for.

The purpose of this project is to measure the set-up deviations μ for pelvic patients, using an electronic portal imaging device (EPID), to calculate the set-up errors $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ and, for the Department of Radiation Physics at the Finsen Centre, Copenhagen, to find the optimal correction strategy to decrease μ.

2. Patient set-up errors

2.1 Definition of set-up deviations

A patient set-up deviation μ is defined as the difference between the actual and intended position of the part of the patient´s body to be irradiated. The intended position is recorded on a reference image, being either a simulator image or a digitally reconstructed radiograph (DRR). This image is then matched with the treatment portal image. Due to mach structures, e.g. anatomical structures, markers or the outline of the field, the set-up deviation, μ, can be measured [1]. These set-up deviations can be described as a sum of the systematic and random contributions [1-6,9-11,16-20]. The systematic component is defined as the difference between the planned patient position and the average patient position if the number of fractions converges towards infinity, but is estimated for a patient by the mean deviation in a given direction. This mean deviation m_p is called the individual systematic set-up deviation, see Eq.1, and the most important factor that systematic deviations can arise from is transfer errors from the simulator or the CT-scanner (were the reference image is created) to the treatment machine. Any other inaccuracies during treatment preparation are a source of systematic displacements, e.g. incorrect placements of skin marks [3,4].

The individual systematic set-up deviation m_p is most often considered to be constant for the patient, i.e. it tends to be the same throughout treatment [6]. If m_p is significant and not properly corrected for, there will be an offset in radiation delivery to the target volume [17].

While investigating a group of patients the systematic error $\Sigma_{set\text{-}up}$ is described by the standard deviation of the m_p distribution, see Eq. 5. These m_p-values are distributed around a mean value called $m_{overall}$, see Eq.3. This mean value is the average of the mean deviations m_p, i.e. the overall mean systematic deviation for all patients. If $m_{overall}$ is significant there is a constant displacement for all patients and the process has to be checked to find the cause of the error. The reason could be differences between the CT and the treatment machine couches or a misadjusted laser [6].

The random component consists of the set-up deviations between different fractions during a treatment session [1]. These random displacements may occur by chance and correspond to day-to-day set-up variations e.g. movements of the tissues or patient during the irradiation or

during the period between the positioning and irradiation [3,17]. Unlike the individual systematic set-up deviation m_p, the individual random set-up deviation $\sigma_{rand,p}$ is not assumed to be constant throughout treatment, which explain why $\sigma_{rand,p}$ is defined as the standard deviation of the individual distribution of the deviations μ for a patient, see Eq.2. The deviations μ distributes around the patient's m_p.

While investigating a group of patients the random set-up error $\sigma_{set\text{-}up}$ is described by the standard deviation of the $\sigma_{rand,p}$ distribution, see Eq. 4.

Because of the non-rigid patient body, random deviations should always be expected. However, if the number of fractions is large, the mean individual random set-up deviation over the course of treatment converges towards zero [2,3]. Large random deviations can be reduced by a better patient immobilisation strategy.

The measured set-up deviation μ also includes errors introduced by the generation of the DRR or digitisation of the portal image caused by a finite sampling resolution [1]. Another type of set-up error is an intra-fraction error, defined as a deviation observed within a single fraction. Periodic movement such as breathing causes this deviation. As these movements during a single fraction are generally negligible for most patients and treatment sites, with a few exceptions of for instance the lung, intra-fraction errors are often neglected [1].

2.2 Determination of systematic and random set-up errors

The mismatch result, i.e. set-up deviation μ, is a deviation combining both random and systematic components. To achieve enough data to separate the two components and determine their relation, multiple images needs to be acquired.

The set-up errors are $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$, and are defined as the standard deviations of the individual systematic and random set-up deviations for all patients, respectively. The reliability of the following statistical approach, that estimates these standard deviations, is depending on the number of patients P and images n_p used in the study. All patients P are assumed to be coherent in terms of set-up technique. The calculation method assumes that both random and systematic components are normally distributed [9]. Numerous studies of localisation displacement support this assumption [7,18].

The symbols used in the following, are explained in Table 1.

Except for some modifications, Table 1 and Eqs. 1-5 can be found in Greener´s "Practical determination of systematic and random set-up errors, $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ using portal imaging" [9].

Symbol	Explanation
i	*Portal image number.*
p	*Patient number.*
$\mu_{(PVI\text{-}DRR)}$	*Deviation between the reference image and the portal image, relative the latter, in a given direction, i.e. the patient's set-up deviation.*
n_p	*Number of images (measurements) taken for patient p.*
N	*Total number of images (measurements) in study.*
P	*Total number of patients for which images were acquired.*
m_p	*Mean deviation for a given parameter for patient p for all images taken i.e. the individual systematic set-up deviation for patient p in a given direction.*
$m_{overall}$	*Overall mean systematic deviation in a given direction i.e. the average of the m_p for all patients P.*
$\sigma_{rand,p}$	*Individual random set-up deviation, i.e. the standard deviation of the distribution of the deviations μ around m_p for a patient p.*
$\sigma_{set\text{-}up}$	*The random set-up error for all patients P in a given direction i.e. the standard deviation of the $\sigma_{rand,p}$ distribution.*
$\Sigma_{set\text{-}up}$	*The systematic set-up error for all patients P in a given direction i.e. the standard deviation of m_p distribution.*

Table 1. Explanation of notation used in Eqs. 1 to 5

Mean deviation of n_p measurements i.e. the individual systematic set-up deviation for patient p:

$$m_p = \frac{1}{n_p} \sum_{i=1,n_p} \mu_{(PVI-DRR),i} \tag{1}$$

Individual random deviation for patient p:
(When i converges towards infinity the mean random deviation is zero by definition.)

$$\sigma_{rand,p} = \sqrt{\frac{1}{n_p - 1} \sum_{i=1,n_p} \left(\mu_{(PVI-DRR),i} - m_p\right)^2} \tag{2}$$

Overall mean systematic deviation for all P patients:

$$m_{overall} = \frac{1}{N} \sum_{p=1,P} n_p \cdot m_p \tag{3}$$

Random se-up error:

$$\sigma_{set-up} = \sqrt{\frac{1}{N-P}\sum_{p=1,P}\sigma^{2}_{rand,p}\left(n_p - 1\right)} \tag{4}$$

Systematic set-up error:

$$\Sigma_{set-up} = \sqrt{\frac{P}{N\left(P-1\right)}\sum_{p=1,P} n_p\left(m_p - m_{overall}\right)^2} \tag{5}$$

If $\Sigma_{set\text{-}up}$ is the unknown standarddeviation of the individual systematic set-up deviations m_p for P patients, t the konstant for the t-distribution with (P-1) degrees of freedom (and at 95 % confidence limit) then the absolute values of $m_{overall} > t \cdot \frac{\Sigma_{set-up}}{\sqrt{P}}$ indicates a statistically significant overall systematic deviation at the 95 % confidence limit and should be investigated [9,21].

2.3 Definition of Time trend

According to Chap.2.1 the individual systematic set-up deviation assumed to be constant for the patient, i.e. m_p tends to be the same throughout treatment. Generally, this is the case. But if the patient loses weight during the course of treatment, or feel more tension confronting the treatment than the preparation and then gradually relaxes, as the number of fractions increases, there could be a presence of a progressive displacement with time. In other words, if the set-up deviation μ, which consists of both the random and systematic part, drifts during the treatment course a time trend is present [1,3,4].

The calculation method in Chap.2.2 assumes that no time trend is present [3]. In the analysis of the set-up deviation as a function of time, the displacements are plotted against time from the first fraction along a specific direction. The slope of the linear fit indicates if there is a significant time trend present [15].

3. Correction strategies

3.1 Definition of a set-up correction strategy

How should a set-up correction be made? Common sense suggests that if a deviation μ is observed, a correction $c = -\mu$ has to be applied. [5] This could be a good correction strategy if there is a possibility to perform a set-up correction at every fraction. Today it is nearly impossible due to the large workload this strategy will cause. To decrease the workload, fewer set-up measurements and corrections has to be made. Because the random part of the deviation is assumed to vary from fraction to fraction, and the fact that μ contains both a random and a systematic contribution, a correction $c = -\mu$ can be incorrect and even introduce a magnification of the individual systematic set-up deviation m_p.

An optimal correction strategy should thus first identify and quantify m_p, and then apply an appropriate correction based on the acquired data [2, 9]. The strategy should also minimize the likelihood of over correction, as it will require further adjustment and increase the workload. The set-up correction can be performed most accurately after a large number of measurements, because for every added measurement the estimation of m_p improves and then the magnitude of the correction converges towards m_p.

On the other hand, there is a need to correct large m_p as early as possible. Any correction procedure is therefore a trade-off between accuracy, workload and the need to apply corrections at an early stage in the treatment [9].

Set-up corrections could be made on-line during treatment or off-line after irradiation. On-line correction means that before irradiation a portal image is acquired and the patient's set-up deviation μ is quantified. Patient set-up is corrected by the total error, $c = -\mu$, if requested. The advantage of this method is that no complicated calculations are needed to get the patient's set-up correction, because the total error can be used. The disadvantage is that the method is time consuming. Because during the measurement the patient is still on the couch and thus the treatment machine is occupied.

An off-line correction means that during irradiation a portal image is acquired and the patient's set-up deviation μ is quantified when the treatment fraction is finished. If required, the patient set-up is corrected by the individual systematic set-up deviation m_p before the next treatment fraction. The advantage is that the workload is modest, since the deviation μ can be

measured any time between two fractions. However, the calculations of the set-up correction could be complicated because the next fraction, which is to be corrected by m_p, contains a different random set-up deviation [12].

The off-line correction method is intended to reduce the individual systematic set-up deviation m_p, which is defined as the mean deviation of the n_p measurements. It is most effective when the random set-up error is small compared to the systematic set-up error i.e. the ratio $\sigma_{set\text{-}up} / \Sigma_{set\text{-}up}$ is small, since it is difficult to correct precisely when the random set-up error is dominant. But if $\sigma_{set\text{-}up}$ is large, a better patient immobilisation strategy and an on-line correction method are to be preferred to reduce large inter-treatment random variations [2, 9]. This work is only considering off-line correction strategies.

3.2 Shrinking Action Level strategy

Bel et al. [2] found a correction strategy that is a compromise between accuracy and an early correction of the individual systematic set-up deviation m_p by defining an action level that shrinks as the number of measurements increases, the SAL (Shrinking Action Level)-strategy [1,2,6].

They use an action level equal to $\alpha / \sqrt{n_p}$ were n_p is the number of measurements and α is the variable initial action level, given in a number j of $\sigma_{\text{set-up}}$, i.e. $j\sigma_{set-up} / \sqrt{n_p}$.

The procedure, see Fig. 1, takes place during the first consecutive number of fractions and the decision to correct a patient set-up or not is made off-line after the irradiation [2].

After each number of measurements an average deviation μ_{SAL} is calculated. If μ_{SAL} is smaller than the action level and the number of given measurement, n_{max}, is not reached, the procedure is continued with a reduced action level. If μ_{SAL} is larger than the action level the set-up is corrected, with a magnitude equal to μ_{SAL}, at the next session. The measurement cycle is then restarted. The procedure is finished when μ_{SAL} is smaller than the action level and n_{max} is reached [2,4,7,11].

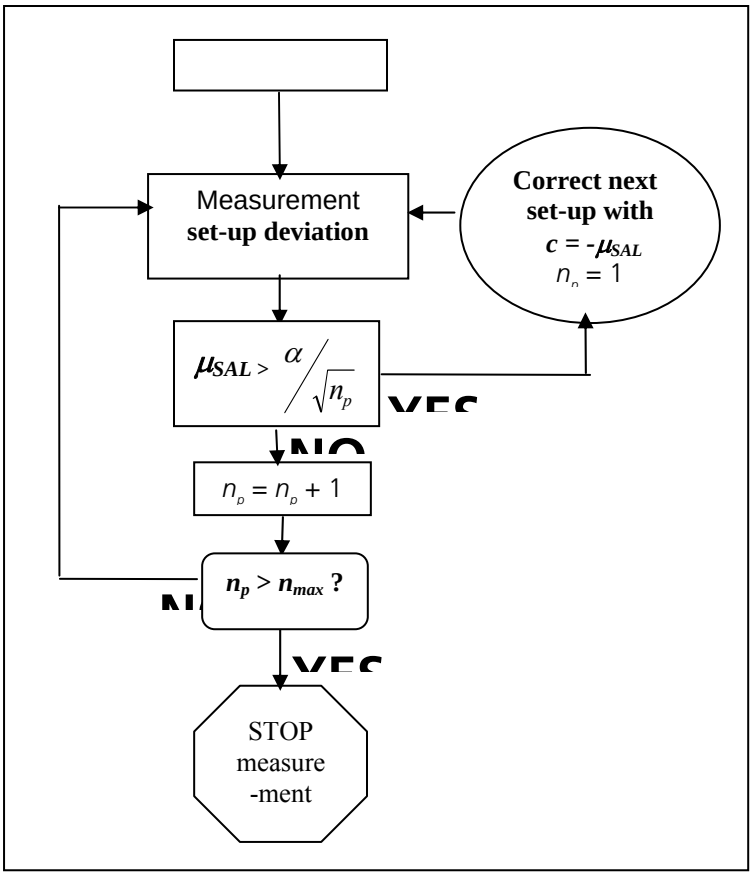

Fig. 1. Shrinking Action Level-procedure schedule.

The combination of the two parameters C(j,n_{max}) will determine the reduction of the individual systematic set-up deviation and the workload, which is expressed as the number of measurement and corrections. Bel et al. [2] found that the three optimal parameter combinations are C(3,4), C(1,1) and C(2,2). Depending on chosen combination for the procedure, the workload results either in a minimum number of corrections, a minimum number of measurements or a compromise between these two [4].

The advantage of SAL is that it avoids a set-up being corrected too early, where deviations observed in the start of treatment arise through random error rather then systematic. However, the method is ineffective. Because when the process is restarted, information obtained before the restart is lost [2,9]. The SAL-strategy is effective first when the random set-up error is large compared to the systematic set-up error i.e. when the ratio $\Sigma_{set\text{-}up}/\sigma_{set\text{-}up}$ is small.

3.3 No Action Level strategy

Boer et al. have introduced the NAL (No Action Level)-strategy [16]. Using this method, the first n_p fractions are imaged and the individual systematic set-up deviation m_p is estimated to be the mean of these measurements m_{NAL} , see Eq. 6.

$$m_{NAL} = \frac{1}{n_p} \sum_{i=1}^{n_p} \mu_i \tag{6}$$

The μ_i is the i:th measured deviation. In the following fractions the correction, c = -m_{NAL}, is always applied, irrespective of the deviations magnitude. The number of measurements per patient is therefore always n_p [9]. An advantage with NAL is that the correction is made at an early stage in treatment. However, when the random set-up error is large compared to the systematic set-up error i.e. the ratio $\sigma_{set\text{-}up} / \Sigma_{set\text{-}up}$ is large, the ability of the NAL-strategy to quickly estimate the patient's systematic set-up error m_p is less successful. To achieve a reasonable estimation, i.e. has m_{NAL} converging towards m_p, more images are required.

3.4 Maximum Likelihood and Adaptive Maximum Likelihood strategy

Shalev et al. [9] introduced a correction strategy involving a correction factor called factor of Maximum Likelihood (ML). The set-up correction to be applied is modified to -$k\mu$ according to Eq. 7.

$$k = \Sigma^2_{set\text{-}up} / (\Sigma^2_{set\text{-}up} + \sigma^2_{set\text{-}up}) \tag{7}$$

Shalev et al. [18] and Gluhchev [5] developed ML to Adaptive Maximum Likelihood (AML) -strategy. This strategy makes use of the accumulated data to determine the required correction -$k\mu_i$, where μ_i is the i:th measured displacement and k is modified according to Eq. 8.

$$k = n_p\Sigma^2_{set\text{-}up} / (n_p \Sigma^2_{set\text{-}up} + \sigma^2_{set\text{-}up}) \tag{8}$$

(When the number of measurements n_p increases, k converges towards 1.)

The AML factor can be implicated in the SAL strategy [4]. When the average deviation μ_{SAL} is larger than the action level, the AML factor is then applied by multiplying k by μ_{SAL} before a correction is made [4,5]. When the set-up deviation is corrected, the value of $\Sigma_{set\text{-}up}$ is recalculated and put back into following calculations to produce an adaptive value of k.

An advantage with the AML is that the factor reduces the possibility of significant over-correction, which can occur if the random set-up error is larger then the systematic one i.e. $\sigma_{set\text{-}up} > \Sigma_{set\text{-}up}$. However, using AML require knowing the values of $\Sigma_{set\text{-}up}$ *and* $\sigma_{set\text{-}up}$.

4. Materials and methods

4.1 Patients group and treatment technique

The patients in this study were treated for bladder-, rectum-, anus- or gynecologic-carcinoma. The total number of patients involved in the determination of the systematic and random errors was 17. All patients were virtually simulated. During treatment preparation a CT scan of the pelvic region was performed and the patients skin was tattooed to indicate isocenter. On the treatment machine, patients were positioned by aligning the tattooed dots with laser beams in the three main directions.

All patients were treated with at least three orthogonal fields with a gantry angel of 0, 90, 180 or 270 degrees. All fields were conformal, defined by a multileaf collimator (MLC). In this study portal images were aquired of the posterior-anterior (PA) and left lateral field at every fraction during the course of treatment. Number of fractions varied from 20 to 28. Two patients did not have a PA treatment field why an anterior-posterior (AP) portal image was taken instead. All shifts in one direction were always given the same sign. In total, 386 PA and 379 lateral portal images were analysed. The portal images system was PortalVision aS500 with an Amorphous Silicon flat panel imager detector type. The DRRs were generated in the Treatment Planning System (TPS) Varian Eclipse and the portal images were acquired in Varian Portal Vision system. The images were then matched and analysed in Varis Vision application.

4.2 Portal image acquisition and matching

In this study the set-up deviation μ was measured by portal image analysis using bony anatomy [10,12]. Digitally reconstructed radiographs (DRRs) were generated in the TPS during planning and used as reference images. The DRRs and the corresponding field outlines were imported into the portal image analysis system. This system used a matching tool that

compares DRR with the current portal image to analyse quantitative field- and patient set-up deviation [12].

In the review environment a transparent layer, upon the DRR, was created. On this "match-anatomy"-layer, a manually drawing of the bony anatomy was made with the freehand drawing option see Fig. 2.

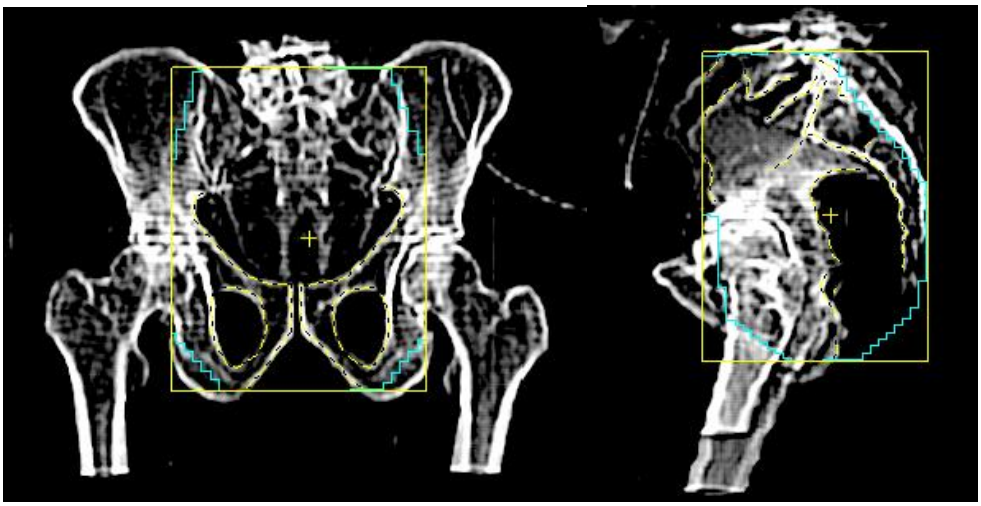

Fig. 2. DRRs of an anterior-posterior field respective of a left lateral field. The yellow broken lines are manually drawings of the bony anatomy. The yellow straight lines correspond to the collimator positions and the blue lines to the field aperture contour.

A layer, only containing a copy of the field aperture contour, was created as well. The field aperture contour is the final field edge and can be generated by the three shielding devices; collimator, MLC or customized block [12].

In the portal image, the field edge and the bony anatomy were detected and matched to the reference drawings and edges, see Fig. 3-4.

In Varians Vision software the match process consists of two procedures. First, the "field edge matching" that is a function that automatically extracts the field edge from the portal image and tries to align the planned field edge (field aperture contour) from the reference image (DRR) with the portal image field edge using chamfer matching [12,13,14].

Secondly, the "anatomy matching" that is working likewise. First the function automatically extracts the anatomy from the portal image using top-hat filter [8,12]. Then it tries to align the anatomy drawing from the DRR with portal image anatomy using chamfer matching. The search algorithm starts from the field edge match and includes translation and rotation. The magnification is kept fixed [12]. If the match result is not satisfying, both the field edge match

and the anatomy match can be adjusted manually. Mismatch result is given in x- and y-direction as well as rotation. In the anterior-posterior field a deviation in the x- direction corresponds to a lateral displacement of the patient. In the left lateral field a deviation in the x- direction corresponds to a vertical displacement of the patient. In the both fields a deviation in the y-direction corresponds to a longitudinal displacement of the patient.

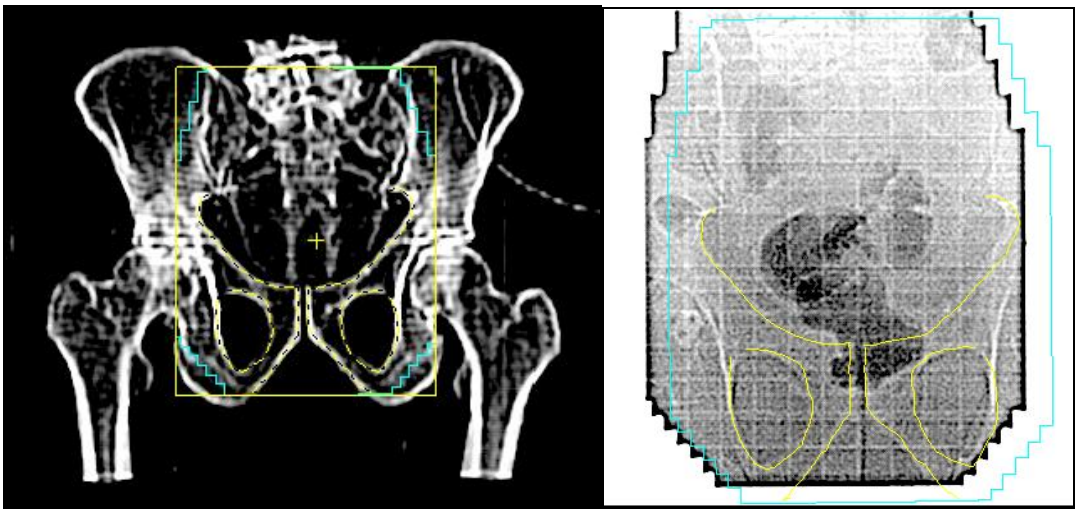

Fig. 3. **The DRR to the left and the math result to the right, where the anatomy structure from the DRR fits optimal with the detected anatomical structures from the portal image. (Images made from an anterior-posterior field)**

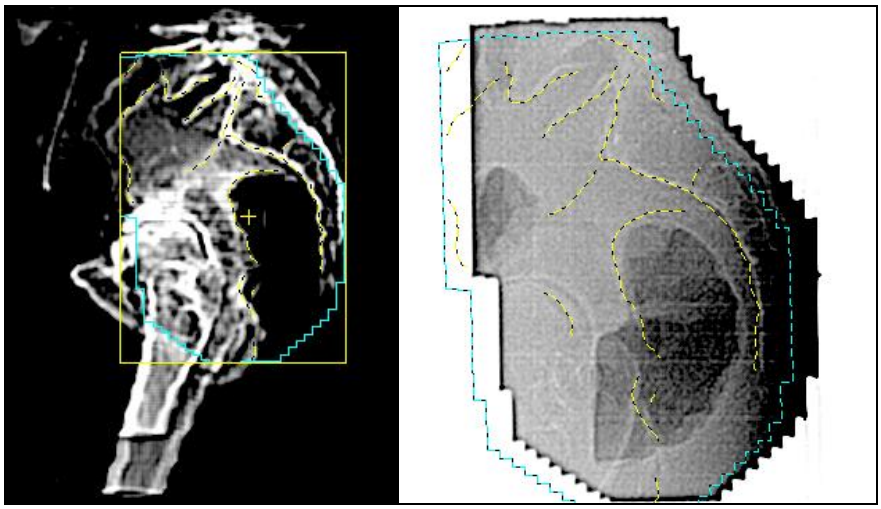

Fig. 4. **The DRR to the left and the math result to the right, where the anatomy structure from the DRR fits optimal with the detected anatomical structures from the portal image. (Images made from the left lateral field)**

As some bony anatomy in the pelvic region is more fixed than others while lying on a couch and as a DRR is a 2D reconstruction of a 3D object, it was important to draw along bony anatomy as it gives the highest accuracy while matching.

For example, patients can move their leg position between the preparation and the treatment session without affect the PTV-location relative the treatment beam. If then, especially in the lateral field, caput femoris, collum femoris or trochanter major is selected as bony anatomy match structure the match result may turn out incorrect.

According to recommendation from an oncologist at the department, linea terminalis, foramen ob tura-torium, pubic bone, incisura ischiadicum and os sacrum are optimal bone structures.

The number of lines that were drawn was not important, as long as there was enough representative anatomy drawn [12].

The DRRs was created from a CT-scan, which radiation is x-rays (kV), while the portal images are made of MV-radiation. The photon's interaction with matter is dependent of their energy. Consequently, an images quality varies with type of radiation. The higher the energy is to acquire an image the lower is it contrast. This explains why the portal image quality was limited. The patient's amount of soft tissue and intestine gas in the treatment area also contributed to reduce the image quality.

To make the anatomy appear sharper a filter was used, see Fig. 5. A Laplacian filter performs an image sharpening, i.e. the operation enhances edges in all directions.

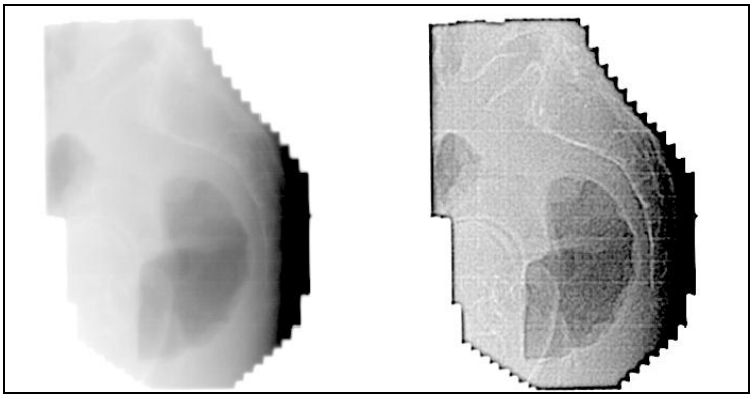

Fig. 5. The original respective filtered portal image on a left lateral field.

Since filters always affect the information in an image, both reference image and its corresponding portal image were filtered before anatomy drawing and matching. The filter used, called "pelvic filter" in the Vision Review menu, is an edge enhancement filter. Since

the chamfer matching function did not work that well, mostly of the field edge match result and anatomy match result had to be adjusted manually. All 765 images were treated equally and only one observer has making the freehand anatomy drawings and match adjustments.
All the deviation data were collected in an Excel file and $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ were calculated, see Eqs. 1-5 in Chap. 2.2.
Once the relation between the $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ was known, it was possible to apply an appropriate correction strategy, see Chap. 3.

4.3 Computer simulated set-up deviations

A computer program simulated set-up deviations μ_S for 1000 "patients" P_S to evaluate different set-up corrections strategies (S=*Simulation*). Every "patient" received 25 fractions each i.e. n_{pS} = 25, which gave total 25 000 set-up deviations. For each patient an individual systematic set-up deviation m_{pS} was created from a normal distribution, and for every image an additional individual random set-up deviation $\sigma_{rand,pS}$ was introduced. This random deviation was generated from another normal distribution. The normal distributions had a standard deviation of $\Sigma_{set\text{-}upS}$ and $\sigma_{set\text{-}upS}$, respectively and the program was written in MATLAB, see fig.10.

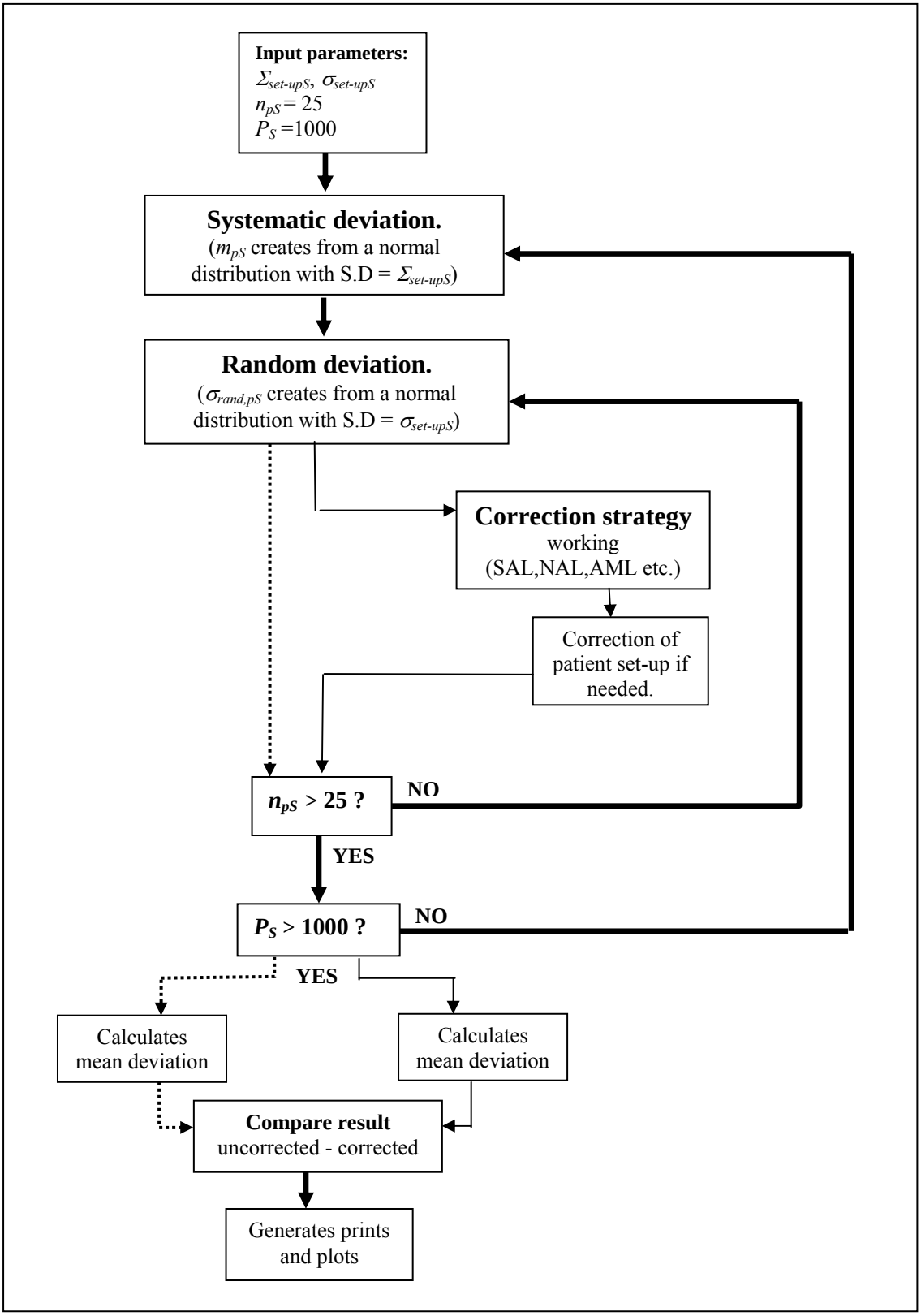

Fig. 10. Flowchart of the computer simulation. For correction strategies, see Chap. 3.

The values of the input parameters $\Sigma_{set\text{-}upS}$ and $\sigma_{set\text{-}upS}$, i.e. the systematic and random error for the group of "patients" P_S, were varied so it could be investigated what strategy was the most appropriate at different conditions. Condition means different relations between the errors. Investigated relations were $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS} / \mathbf{2}$, $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$, $\Sigma_{set\text{-}upS} = \mathbf{2}\sigma_{set\text{-}upS}$ and $\Sigma_{set\text{-}upS} = \mathbf{3}\sigma_{set\text{-}upS}$. According to Bel et.al [2] and Bijhold et.al [17] the first relation is not likely to occur in clinical practice, although the author of this work decided to investigate this unusual relation.

The simulation was then used to compare different strategies with each other and to find the most accurate correction strategy for this particular group of patients on this department. The simulated strategies were SAL, NAL and the current strategy (at the department). It was assumed that the AML factor could be implicated to any kind of correction strategy, why mixtures including AML also were simulated. For the NAL strategy the AML factor was applied by multiplying the mean value m_{NALS} of the first n_{pS} measurements by AML before following fractions were corrected.

The parameter combinations, j_S and n_{maxS}, involved in the SAL simulations was equal to C(1,1), C(2,2) and C(3,4). The simulation verified the number of measurements and corrections per patient for the different combinations. The different correction strategies efficiency was measured by comparing the mean deviation for the absolute value of all positions before and after correction. As a last step the clinical investigated values of $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ were put into the chosen optimal strategy, based on the computer-simulated results, to find out how much the mean deviation could be reduced for the clinically investigated patients if the optimal strategy had been used instead of the current one.

Possible time trends during the course of treatment were not incorporated in the simulated study.

5. Results and discussion

5.1 Simulation results: Finding optimal correction strategy

With the simulated "patient's" generated deviations μ_S different correction strategies were investigated with varied relations between $\sigma_{set\text{-}upS}$ and $\Sigma_{set\text{-}uSp}$. The mean deviation for all positions before and after correction was compared, see Table 2.

The simulated study showed that among all investigated correction strategies and for all relations between $\Sigma_{set\text{-}upS}$ and $\sigma_{set\text{-}upS}$ it is always most successful to chose the No Action Level (NAL) strategy with Adapted Maximum Likelihood (AML) method. The optimal number of measurements n_{pS} to perform before the average m_{NALS} is calculated is depending of the departments´ resources. According to the simulated results the reduction of the mean deviation is greater when the number of measurements n_{pS} is increased from 2 to 3 than from 3 to 4, see Table 2.

Greener et.al [9] declare that the number of measurement has to increase even more to achieve a reasonable estimation of the individual systematic set-up deviation m_p if the individual random set-up deviation $\sigma_{rand,p}$ is very dominant. This was not tested since more than 4 measurements is not relevant according to the increased workload.

Multiplying any correction strategy with AML resulted in a reduction of the mean value. It was most significant when the random set-up error was larger than the systematic i.e. $\Sigma_{set\text{-}upS} < \sigma_{set\text{-}upS}$.

According to Bel et. al [2], the Shrinking Action Level (SAL) strategy has three optimal combinations of j and n_{max}, namely C(1,1), C(2,2) and C(3,4). This was the reason why these were chosen to investigate. Independent of the selected combination, SAL only showed an improved effect when the systematic set-up error was larger then the random set-up error i.e. $\Sigma_{set\text{-}upS} > \sigma_{set\text{-}upS}$. But even when the SAL strategy is most effective within the limit of this simulation, i.e. when the systematic set-up error is 3 times larger then the random set-up error, the NAL strategy is more than twice as good with only 2 measurements.

Unexpectedly, the current strategy did not reduce the mean deviation after correction if systematic and random set-up errors were equal i.e. $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$.

Correction strategy	Reduced mean deviation after correction [%]			
	$\Sigma_{set\text{-}up} = \sigma_{set\text{-}up} / 2$	$\Sigma_{set\text{-}up} = \sigma_{set\text{-}up}$	$\Sigma_{set\text{-}up} = 2\sigma_{set\text{-}up}$	$\Sigma_{set\text{-}up} = 3\sigma_{set\text{-}up}$
Current	-39	0	23	30
Current · AML	6	1	25	33
SAL C(1,1)	-41	0	24	32
SAL C(1,1) · AML	0	12	25	32
SAL C(2,2)	-13	0	24	33
SAL C(2,2) · AML	0	10	24	32
SAL C(3,4)	0	0	17	27
SAL C(3,4) · AML	1	2	18	27
NAL $n_p = 2$	-40	31	64	76
NAL ($n_p = 2$) · AML	19	43	67	78
NAL $n_p = 3$	-16	42	71	81
NAL ($n_p = 3$) · AML	25	52	72	81
NAL $n_p = 4$	0	51	75	84
NAL ($n_p = 4$) · AML	29	54	76	84

Table 2. Reduced mean deviation [%] after correction with different strategies. A negative result indicates an increased mean deviation after "correction".

The most common relation between the systematic and random set-up errors regarding general pelvic treatment is $\Sigma_{set\text{-}up} = \sigma_{set\text{-}up}$ [1,2,19,20]. For some of the correction strategies the simulated results for this relation are demonstrated in histograms that give the distribution of the absolute mean deviations per patient, see Fig.11-15. The results are compared to the uncorrected one. The narrower a histogram distribution is after correction, the more effective the correction strategy is.

The current strategy

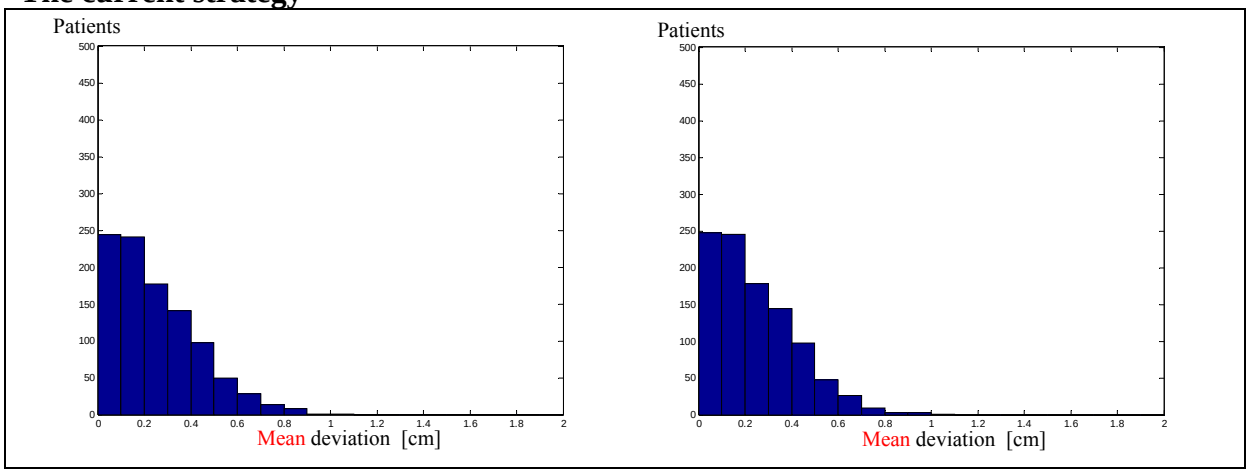

Fig. 11 **No correction $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$** **Current strategy $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$**

The Shrinking Action Level (SAL) strategy (C(2,2))

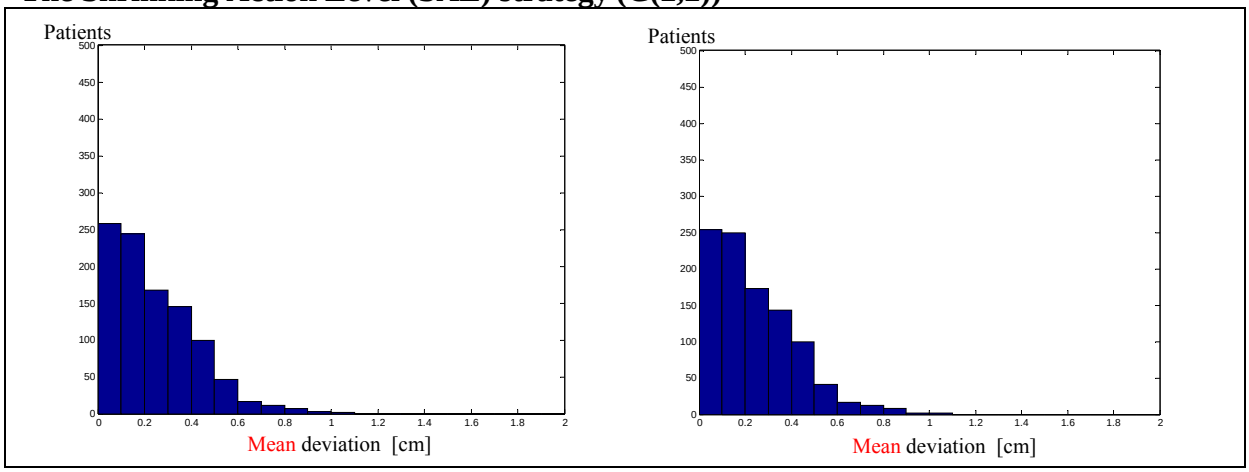

Fig. 12 **No correction $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$** **SAL strategy $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$**

The Shrinking Action Level (SAL) strategy with AML (C(2,2))

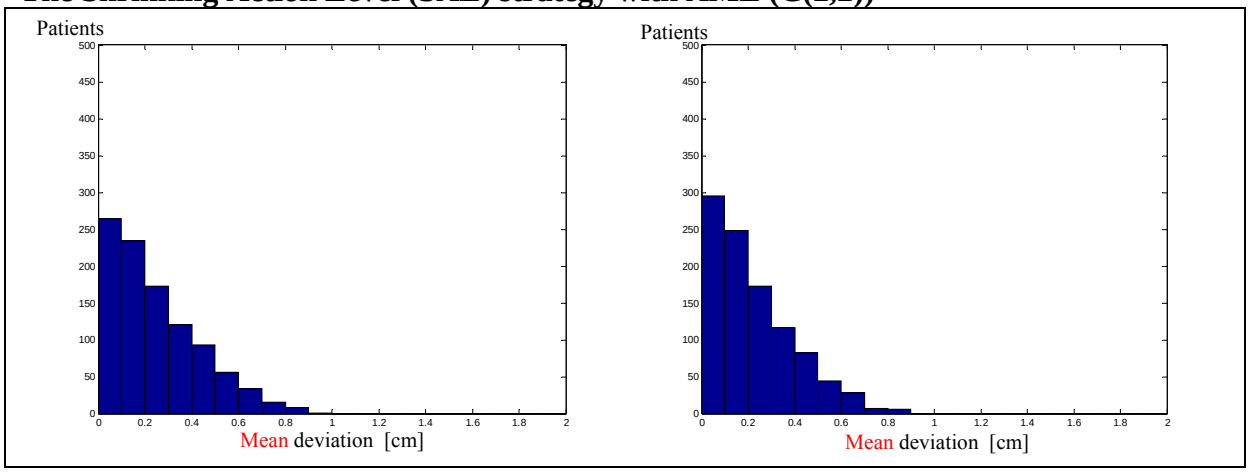

Fig. 13 **No correction $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$** **SAL·AML strategy $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$**

The No Action Level (NAL) strategy (m=3)

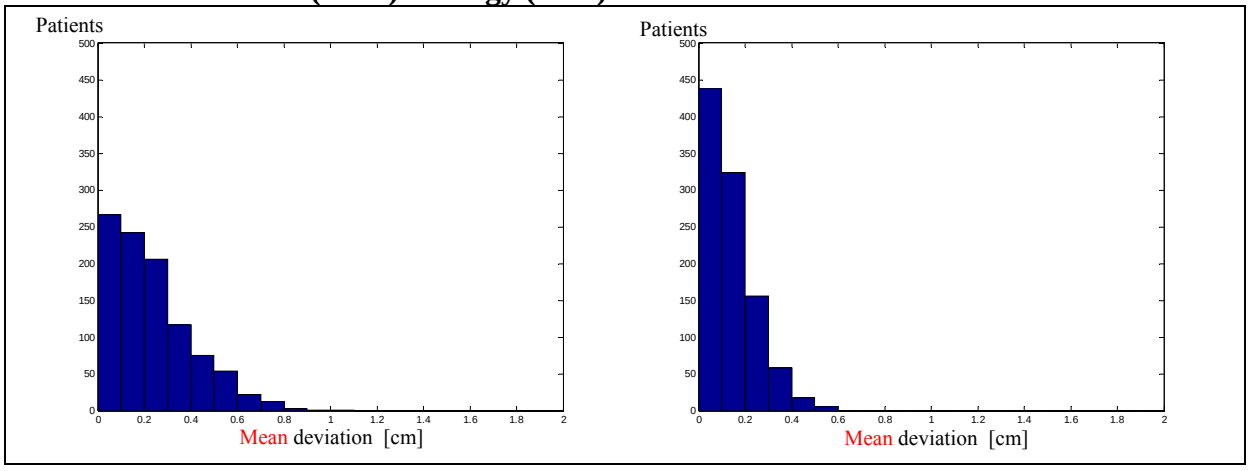

Fig. 14 **No correction $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$** **NAL strategy $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$**

The No Action Level (NAL) strategy with AML (m=3)

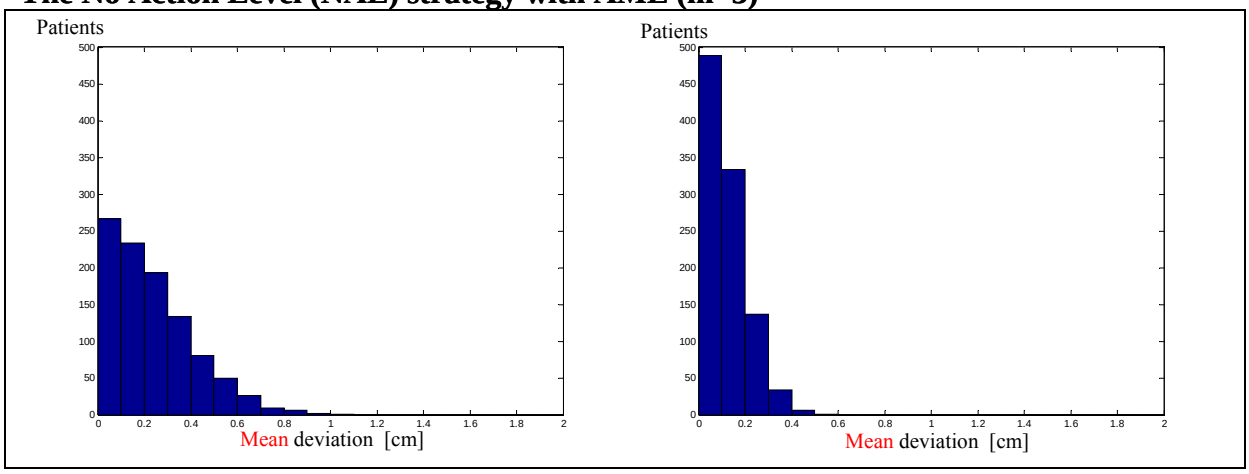

Fig. 15 **No correction $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$** **NAL·AML strategy $\Sigma_{set\text{-}upS} = \sigma_{set\text{-}upS}$**

5.2 Clinical data results: Determination of the relation between $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$

For each patient and each fraction a deviation μ was measured between the reference image and the portal image. The deviations, measured in 381 PA-field images and in 374 lateral field images, were given as a lateral longitudinal and vertical longitudinal displacement, respectively of the patient.

In Fig.16-17 scatter plots illustrates the 2-D displacement vectors by blue cross in the PA-field and the lateral field, respectively. The yellow squares indicate the mean deviation for each patient and the red circles indicate the deviation at the first fraction for each patient. The action level on 5 mm is also shown.

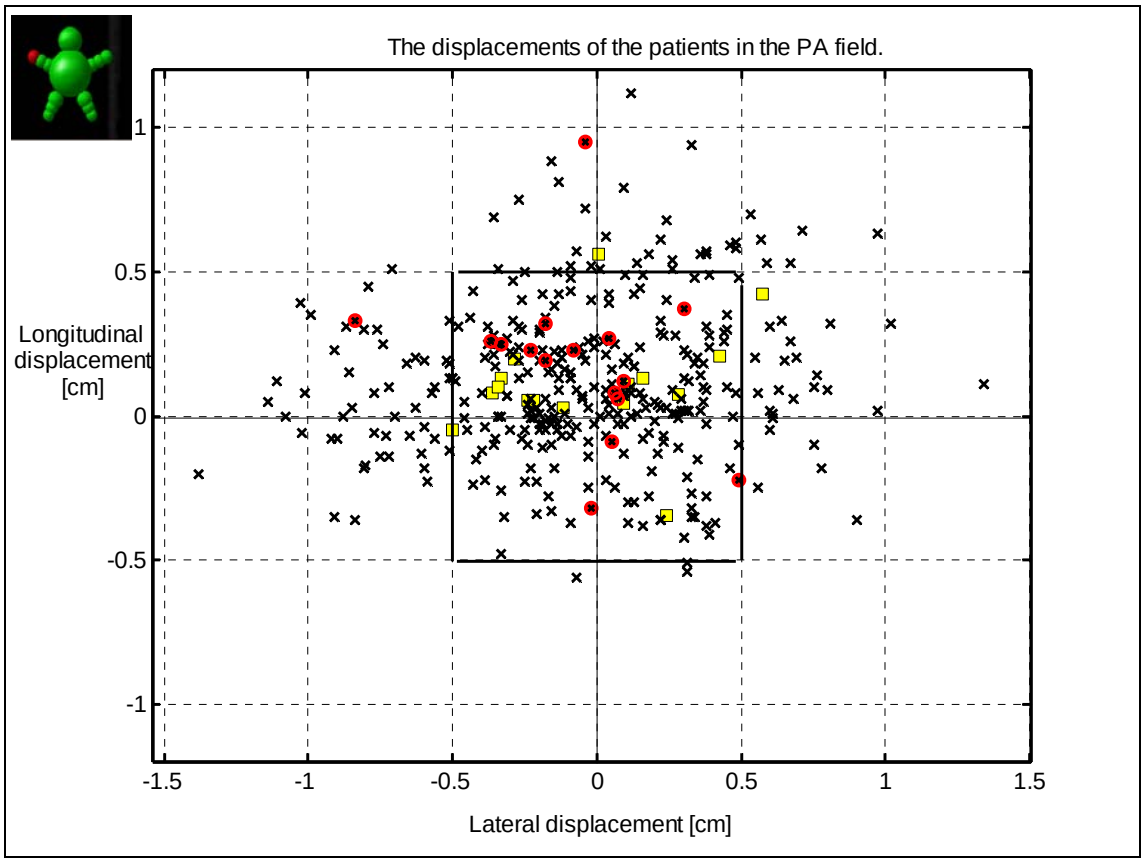

Fig. 16. Scatter plot illustrating the 2-D displacement vectors in the PA-field. Cross = measured deviation. Square = mean deviation. Circle = deviation at first fraction.

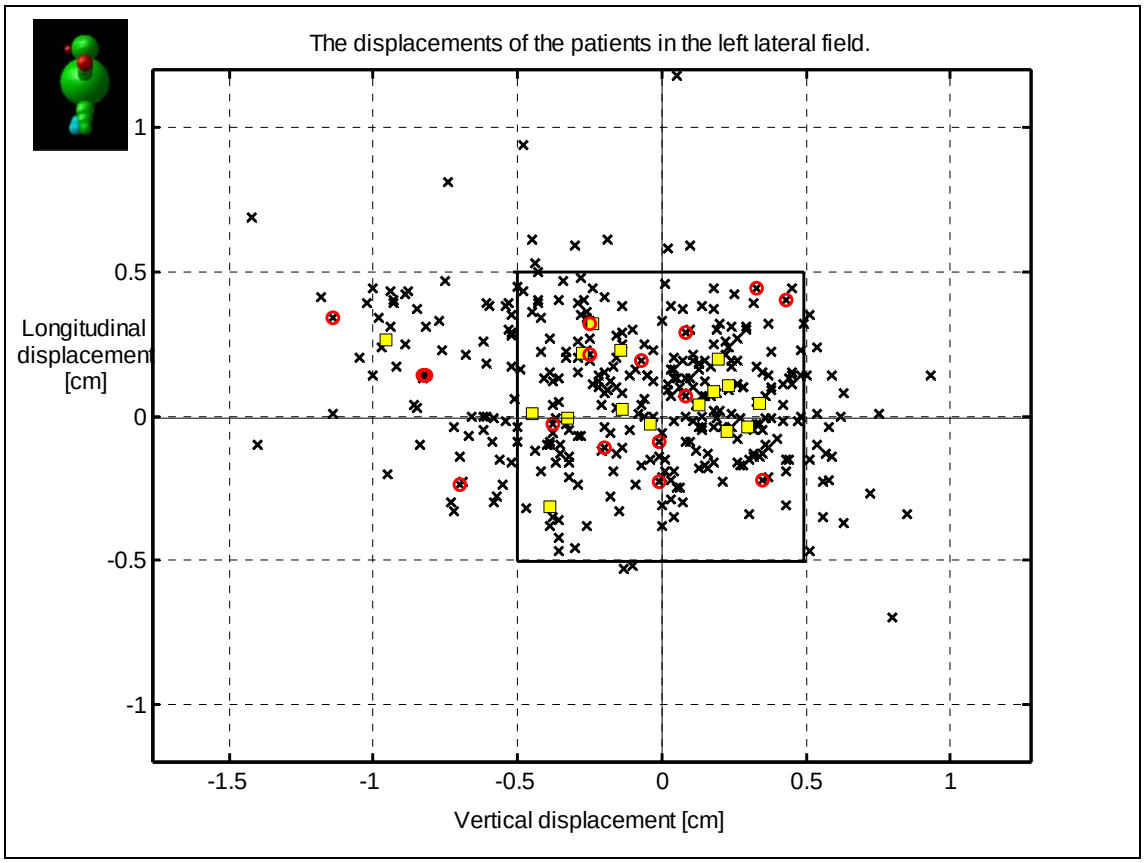

Fig. 17. Scatter plot illustrating the 2-D displacement vectors in the left lateral field. Cross = measured deviation. Square = mean deviation. Circle = deviation at first fraction.

For the set-up deviation measured in the PA-field the mean deviations, i.e. the patients individual systematic set-up deviation m_p, see Eq.1 Chap. 2.2, ranged from -5,2 to 5.7 mm in the left right lateral direction and from -3.5 to 5.6 mm in the caudal cranial longitudinal direction. In the lateral field the m_p ranged from -9.5 to 3,1 mm in the dorsal ventral vertical direction and from –3,2 to 3.3 mm in the caudal cranial longitudinal direction. In the PA-field the individual random set-up deviation $\sigma_{rand,p}$, see Eq.2, ranged from 1.3-5.5 mm in the left right lateral direction and from 1.1-3.5 mm in the caudal cranial longitudinal direction. In the lateral field $\sigma_{rand,p}$ ranged from 1.3-4.5 mm in the dorsal ventral vertical direction and 1.2-3.8 mm in the caudal cranial longitudinal direction.

The overall mean systematic deviation, $m_{overall}$, was calculated according to Eq. 3. The random set-up error $\sigma_{set\text{-}up}$ i.e. the standard deviation of the $\sigma_{rand,p}$ for all patients, was calculated according to Eq. 4 and the systematic error $\Sigma_{set\text{-}up}$ i.e. the standard deviation of the m_p for all patients, was calculated according to Eq.5. The results are showed in Table 3.

The mean rotation in the PA-field ranged from 0-0,53 degree with a standard deviation of 0,12 degree. The mean rotation in the lateral field ranged from 0,1-1,28 degree with a standard deviation of 0,30 degree. These small rotations have a negligible impact on the derived systematic and random set-up errors.

Field	**Posterior-Anterior (PA) 180°**		**Left lateral 90°**	
Direction	left right lateral	caudal cranial longitudinal	dorsal ventral vertical	caudal cranial longitudinal
$m_{overall}$ [mm]	-0.62	0.90	-1.08	0.69
$\sigma_{set\text{-}up}$ [mm]	3.13	2.02	2.85	2.13
$\Sigma_{set\text{-}up}$ [mm]	3.12	2.18	3.32	1.56

Table 3. Uncorrected results

The results showed that the systematic set-up error was approximately equal to the random set-up error in all four cases.

To decide whether the overall mean systematic deviation, $m_{overall}$, was significant a t-test was performed [21]. The 17 (P=17) mean deviations m_p were assumed to follow a t-distribution with standard deviation equal to $\Sigma_{set\text{-}up}$. The degrees of freedom were 16 (df= P-1). For a 95 % confidence level and 16 degrees of freedom the tabulated t-constant is 2.12 [21]. Since the absolute value of $m_{overall} < 2.12 \cdot \frac{\Sigma_{set-up}}{\sqrt{17}}$ in all 4 cases there was no indication of a statistically

significant overall systematic deviation, at the 95 % confidence level [21]. If $m_{overall}$ had turned out to be significant, then the process had to be checked to find the cause of error. (One reason could be differences between the CT and treatment machine couches.)

To test the accuracy of the matching procedure, the patient's longitudinal displacement in the lateral image was compared to the longitudinal displacement in the PA image. Theoretically these deviations should be equal, since the patient does not move while the treatment machine switch from 180 to 90 degrees. Practically the patient could move accidentally between the two field treatments or be in different phase in their breathing cycle.
Since the number of values (differences between the deviations in the two images for all patients and fractions) was as large as 374, a normal distribution was a god estimation. The mean value was calculated to 0.45 mm and the standard deviation to 1.5 mm.
This means that, at a 95% confidence level, all the deviations between the longitudinal displacement between the lateral and PA images were within the interval 0.45±0.15 mm (z-test: $0.45 \pm 1.96 \frac{1.5}{\sqrt{379}}$ mm). This indicates that no significant systematic mistake has been introduced while performing the matching procedure.

5.3 Application of optimal correction strategy

Once the random and systematic errors, $\sigma_{set\text{-}up}$ and $\Sigma_{set\text{-}up}$, for the investigated patient group were determined, they were put into the optimal correction strategy. Result from the simulated study showed that the most adequate correction strategy for the current relation between $\sigma_{set\text{-}up}$ and $\Sigma_{set\text{-}up}$, is No Action Level (NAL) with Adaptive Most Likelihood (AML) strategy with three measurements, see Table 2, Chap. 3.2. The similar correction strategy, with four measurements instead, gave an even better result but the improvement was small compared to the increased workload.
The NAL(3) ·AML strategy was applied to the treated patients deviation data to investigate how the deviations could have been reduced if this strategy had been implemented at this department. NAL(3) was calculated according to Eqs. 6 with $n_p = 3$ and AML was calculated according to Eq. 8 with values of $\Sigma_{set\text{-}up}$ and $\sigma_{set\text{-}up}$ equal to Table 3.
For the corrected set-up deviation measured in the PA-field, the patients individual systematic deviation m_p, ranged from –2,6 to 2.8 mm in the left right lateral direction and from –1,4 to

1.1 mm in the caudal cranial longitudinal direction. In the lateral field m_p ranged from –2,0 to 2.4 mm in the dorsal ventral vertical direction and from -0.9 to 0.7 mm in the caudal cranial longitudinal direction.

The corrected overall mean systematic deviation, $m_{overall,}$ and $\Sigma_{set\text{-}up}$, are shown in Table 4. The corrected deviation data is illustrated in Fig. 18 and 19.

Field	**Posterior-Anterior (PA) 180°**		**lateral 90°**	
Direction	left right lateral	caudal cranial longitudinal	dorsal ventral vertical	caudal cranial longitudinal
$m_{overall}$ [mm]	0,27	-0,25	0,32	0,047
$\Sigma_{set\text{-}up}$ [mm]	1,45	0,70	1,27	0,46

Table 4. Result after applying NAL(3) AML strategy.

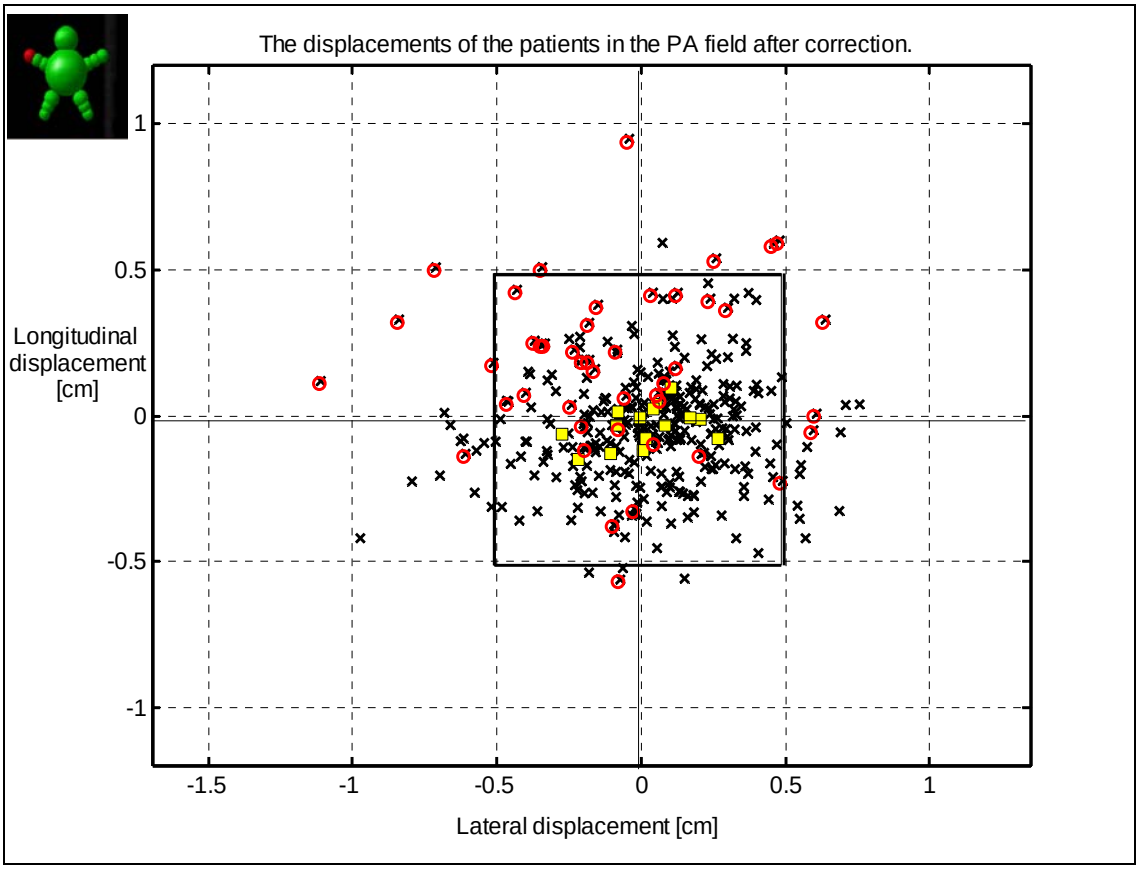

Fig. 18. Scatter plot illustrating the 2-D displacement vectors after correction in the PA-field. Star = measured deviation. Square = mean deviation. Circle = deviation at first 3 fractions.

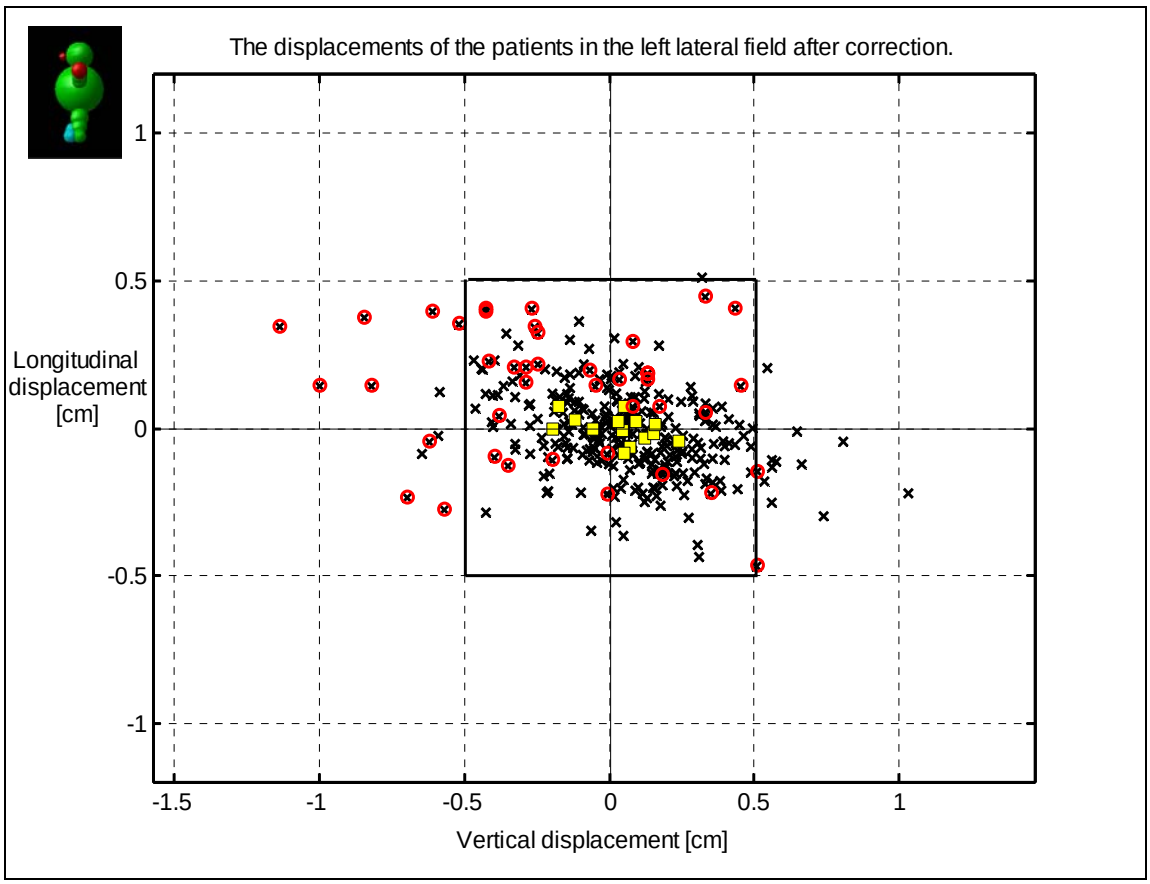

Fig. 19. Scatter plot illustrating the 2-D displacement vectors after correction in the lateral field. Star = measured deviation. Square = mean deviation. Circle = deviation at first 3 fractions.

When the treated patients deviation data, $\sigma_{set\text{-}up}$ and $\Sigma_{set\text{-}up,}$ respectively (see Table 3), were used as input parameters in the same computer simulation that was used to find the optimal correction strategy, the reduction of the mean deviation after the correction was calculated to 49 % in left right lateral direction and 51 % in the caudal cranial longitudinal direction for the PA field. For the left lateral field the reduction was calculated to 55% in the dorsal ventral vertical direction and 38 % in the caudal cranial longitudinal direction. Just 38% is caused by the fact that the systematic error is smaller than the random error and that NAL(3) ·AML strategy gives a greater reduction when the ratio $\Sigma_{set\text{-}up} / \sigma_{set\text{-}up}$ is large.

5.4 Time trend result

In the analysis of the set-up deviations μ as a function of time, the set-up deviations for each of the 17 patients were plotted against time from the start of the treatment. The slope of the linear fit indicates if there is a significant time trend present. Each patient's slope was multiplied with the number of fractions n_p. The resulting total deviation from the start to the

stop of treatment, $\mu_{time,p}$, was then compared to the patient's individual standard deviation of the random set-up error, $\sigma_{rand,p}$.

For 6 patients the $1\sigma_{rand,p} < \mu_{time,p} < 2\sigma_{rand,p}$, but only 1 patient had a $\mu_{time,p} > 2\sigma_{rand,p}$ ($\approx$ 2,4 $\sigma_{rand,p}$). The mean slope for all investigated patients measured 0,021 in the left right lateral direction and –0,024 in the caudal cranial longitudinal direction in the PA field, and 0,057 in the dorsal ventral vertical direction and 0,023 in the caudal cranial longitudinal direction in the lateral field. The results indicated that the set-up errors did not significantly drift during the treatment courses, i.e. the estimation that no time trend was present was acceptable.

6. Conclusion

For the investigated group off pelvic patients the standard deviation of the individual systematic set-up deviations m_p is approximately equal to the standard deviation of the individual random set-up deviations $\sigma_{rand,p}$, i.e. $\Sigma_{set\text{-}up} = \sigma_{set\text{-}up}$.

There is no significant overall mean systematic deviation $m_{overall}$. A computer-simulated study showed that the optimal correction theory is the No Action Level (NAL) strategy with 3 measurements, n_p=3 and with the Adaptive Maximum Likelihood (AML) factor included. Assuming a normal distribution of systematic and random deviations, respectively, an unexpected result from the simulated study is that the current strategy employed in the department does not reduce the mean deviation at all after correction.

When applying the new optimal correction strategy, NAL(3) ·AML, to clinical data, i.e. the treated pelvic patients deviation data, the deviations are effectively reduced after correction. In the PA field the standard deviation of systematic set-up error**,** $\Sigma_{set\text{-}up}$, decreases from 3,12 to 1,45 mm in the left right lateral direction and from 2,18 to 0,70 mm in the caudal cranial longitudinal direction. In the lateral field $\Sigma_{set\text{-}up}$ decreases from 3,32 to 1,27 mm in the dorsal ventral vertical direction and from 1,56 to 0,46 mm in the caudal cranial longitudinal direction, see Table 5.

Uncorrected results [mm]				
Field	Posterior-Anterior (PA) 180°		Left lateral 90°	
Direction	left right lateral	caudal cranial longitudinal	dorsal ventral vertical	caudal cranial longitudinal
Min. deviation	-5.2	-3.5	-9.5	-3.2
Max. deviation	5.7	5.6	3.1	3.3
$m_{overall}$	-0,62	0.90	-1.08	0.69
$\sigma_{set\text{-}up}$	3.13	2.02	2.85	2.13
$\Sigma_{set\text{-}up}$	3.12	2.18	3.32	1.56
Result after applying NAL(3) AML strategy [mm]				
Min. deviation	-2.6	-1.4	-2.0	-0.9
Max. deviation	2.8	1.1	2.4	0.7
$m_{overall}$	0.27	-0.25	0.32	0.05
$\Sigma_{set\text{-}up}$	1.45	0.70	1.27	0.46

Table 5. Summary of uncorrected and corrected results.

As a result of this work a new set-up correction strategy will be implemented for pelvic patients at the Department of Radiation Physics at the Finsen Centre, Copenhagen University Hospital.

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Sofie

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Appendix

Margins

M. van Herk et al. [10] describes a two-stage approach to defining treatment margins. The first stage, “treatment preparation”-stage, is to determine a volume large enough to encompass the mean position of CTV for 90 % of cases. This volume is called the systematic target volume, STV, and is supposed to include all uncertainties that result in a systematic deviation for a given patient, e.g. doctor’s delineation error, phantom transfer error and systematic set-up error. The second stage, the “treatment execution”-stage, is to add an uncertainty to STV, based on inter-fractional (random) organ motion and set-up deviations. The width of this margin characterizes the Gaussian width of the random uncertainties. By adding these two margins to CTV the planning target volume, PTV, is produced, see Fig. 19. The systematic and random deviations are assumed to be generally normally distributed with standard deviations Σ_i respective σ_j, where i and j represents a given source of uncertainty.
The size of the margin, when using a minimum dose limitation, is independent of the CTV size [10]. Due to M. van Herk´s two-stage recipe the impact systematic (treatment preparations) deviation and random (execution) variations is fully separated. It is therefore possible to use separate tables for the two margins. In the same paper M. van Herk show that larger random deviations lead to a small under dosage for most patients, while larger systematic deviation lead to a large under dosage for a small fraction of the patients. The margin recipe, $2{,}5\Sigma + 1{,}64\sigma$, ensures 95% minimum dose to the CTV for 90% of the patient population. In general, the margin for systematic deviations is much larger than the margin for random variations. Also, there is no single deviation that dominates, which means that it is hazardous to reduce a margin based only on improved accuracy of one aspect of the treatment, such as set-up error. If so, it could lead to serious under dosage of the CTV.

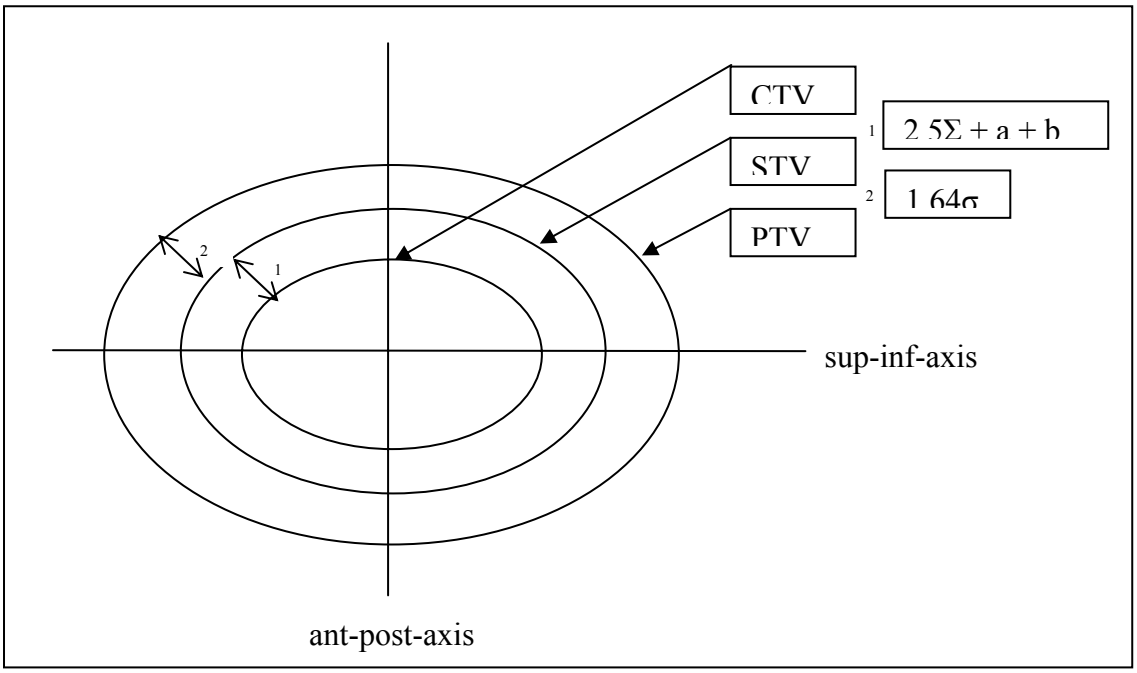

Fig. 19. Derivation of the CTV-PTV margin. "a + b" are two linear errors which correspond to the photon beam algorithm error respective breathing oscillation [6,10].