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Original Article

Is adaptive treatment planning in multi-catheter interstitial breast brachytherapy necessary?

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ABSTRACT

Purpose: For 55 patients treated with interstitial multi-catheter breast brachytherapy the need for adaptive treatment planning was assessed.
Methods and materials: For all patients a treatment planning computed tomography (CT) and a follow-up CT were acquired and used for the retrospective evaluation. Keeping dwell time and dwell positions constant, the treatment plan assessed directly after catheter implantation was compared to the situation 48 h after implantation. Both manual catheter reconstructions, based on the planning and follow-up CT, were rigid registered to each other and the resulting deviations analyzed, like the difference between corresponding dwell positions (ΔDP) or the discrete Fréchet distance. Further, the dosimetric changes, e.g., coverage index (ΔCI), conformal index (ΔCOIN) and dose non-uniformity ratio (ΔDNR) were considered for a deformed planning target volume (PTV) and the rigid warped PTV structure. The PTV was deformed according to the vector field estimated between the two acquired CTs.
Results: Over all patients with rigid aligned CTs a mean ΔDP, ΔCI, ΔCOIN and ΔDNR were determined to 2.41 ± 1.73 mm, 3.10 ± 3.17%, 0.009 ± 0.007 and 0.036 ± 0.040, respectively. Considering the deformed PTV ΔCI was estimated to 5.05 ± 4.14 %.
Conclusion: In conclusion, in 4% of the cases re-planning would have been beneficial to ensure the planned dose delivery. Large PTV changes or large DP deviations were found to be the main reasons for dosimetric variations.
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A common treatment option for breast cancer patients is accelerated partial breast irradiation (APBI) often applied in form of high dose-rate (HDR) multi-catheter interstitial brachytherapy (iBT). The therapy outcome proved to be comparable to other treatment options, such as whole breast irradiation or a percutaneous APBI treatment, with regards to local recurrence rate, disease free survival, overall survival, quality of life, late side effects, toxicity and cosmetic outcome [1–8]. APBI using multi-catheter iBT is defined as irradiation to a predefined clinical target volume encompassing the tumor bed and a surgical margin without any additional margin for planning uncertainties. Due to steep dose gradients inside and outside the implant, it is especially important to ensure the planned dose delivery, to avoid local overdosage, loss of coverage or underestimated dose to the organs at risk [9,10].

Usually, treatment planning in iBT is performed image guided with a single CT acquisition being the standard prior to the first fraction for treatment planning. An additional follow-up CT in the time of the therapy verifies the tissue conformity, proves the stability of the applicator and offers the possibility of adaptive treatment thus increases the precision of the therapy.

The study conducted by Altman et al. [11] investigated the need for re-planning after 24–72 h for strut-adjusted volume implants (SAVI) and found that 64.5% of 62 considered patients did not need an adjusted treatment plan. Scanderbeg et al. [12] proved that after 24 h the tissue conformance is recuperated. These investigations were intensively performed for partial breast irradiation using SAVI but rarely analyzed for multi-catheter breast iBT, where usually the planning CT is acquired around 2 h after implantation and the first fraction is irradiated less than approximately 6 h. Kandasamy et al. [13] compared the planning CT situation to a repeated CT scan acquired after the 6th fraction. Taking 14 patients into account, they estimated a catheter displacement smaller than 3 mm and a 3% change within the D_{90} of the planning target volume.

In order to ensure the planned dose delivery and to obtain the possibility for adapting the treatment plan, at the University Clinic Erlangen since June 2017 an additional computed tomography image (CT) is acquired after the fourth fraction in the middle of

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the treatment schedule. The presented study analyzes the necessity for adaptive treatment planning and estimates dosimetric and geometrical changes between treatment planning CT (PCT) and follow-up CT (FCT) acquired approximately 48 h after implantation using rigid and deformable image registration.

Materials and methods

Patient cohort

Patients treated with HDR iBT APBI between June 2017 and May 2019, which received a follow-up CT (FCT) approximately 48 h after catheter implantation, were included in the study. In total the data of 55 breast cancer patients were included in the evaluation, see Table 1 for details. The patients were treated with 9 fractions, usually Monday to Friday, and received two fractions at least 6 h apart from each other of 3.8 Gy per day.

Approximately 1 h after catheter implantation (flexible plastic tube, 6F, single leader, 30 cm, Elekta, Veenendaal, The Netherlands), the planning CT (PCT) images were acquired using a SOMATOM Sensation open system (Siemens Healthcare GmbH, Erlangen, Germany) with the following routine: axial thorax routine, resolution 0.38 * 0.38 * 2 mm^3, 120 kV, B31s kernel. In 22 of the 55 cases the CT images were recorded in expiration, whereas all other CT images were acquired in free-breathing.

Target delineation and treatment planning were performed image based according to the GEC-ESTRO guidelines [14–16], such that all dosimetric requirements for the target volume and organs at risk (OAR), e.g., skin and ribs, were fulfilled. For both tasks the treatment planning system (TPS) Oncentra Brachy (Version 4.5.3, Elekta, Veenendaal, The Netherlands) was used. The dwell positions (DPs) were activated continuously with a step size of 2.5 mm, an offset of −5 mm and an indexer length of 1287.5 mm. The patients were irradiated using a microSelectron afterloader (Elekta, Veenendaal, The Netherlands). For additional quality assurance, the FCT with the same settings as the PCT was acquired approximately 48 h after implantation, subsequent to the fourth fraction.

Table 1
Patient specifications.
HDR = high-dose-rate; PTV = planning target volume; CI = coverage index; DNR = dose non-uniformity ratio; COIN = conformal index.

Parameter	Specification	Value
Number of patients	Total	55
	Left breast	32
	Right breast	23
	$CT_{Expiration}$	22
	$CT_{Free\text{-}Breathing}$	33
Age	Range	37–83 years
	Median	64 years
Recruitment time		19/06/2017–20/05/2019
Number of catheters	Range	12–27
	Median	17
	Total	963
Catheter length	Range	24.55–157.10 mm
	Median	78.26 mm
	Mean	80.51 mm
PTV	Range	18.07–162.86 ccm
	Median	72.42 ccm
	Mean	18.07 ccm
Breast volume	Range	120.08–1958.70 ccm
	Median	611.74 ccm
	Mean	668.82 ccm
CI	Range	90.31–97.51%
	Median	94.74%
	Mean	94.18%
DNR	Range	0.20–0.31
	Median	0.25
	Mean	0.25
COIN	Range	0.53–0.81
	Median	0.68
	Mean	0.67

Quality assurance routine

Immediately after follow-up CT acquisition prior to the subsequent irradiation, for each patient variations between PCT and FCT were assessed and ensured that the treatment plan still fits to the changed situation. The catheter traces were again reconstructed in the FCT and the OARs, skin and ribs, were recontoured. Both geometrical deviations between the catheter traces and possible influence on the dosimetric quality indices, keeping DPs and dwell times (DTs) constant, could be determined.

The acquired FCT was rigidly registered to the PCT using the registration algorithm integrated into the TPS. Prior performing the registration, the field of view was limited to the region of the breast, such that the influence of breathing phases, varying arm positions or different field of views was reduced. The quality of the registration was verified visually. For the estimation, DPs and DTs were copied from the original treatment plan and applied to the new catheter reconstruction. Following, the planning target volume (PTV) defined on PCT for treatment planning was resampled into the registered FCT (then referred to as PTV_F) and the dosimetric quality indices (QI), such as coverage index (CI), dose non-uniformity ratio (DNR), conformal index (COIN) and the exposure on the OARs, were assessed.

In order to detect possible changes, the distance between the catheters was checked in a randomly chosen subset of 4–6 catheters, the consistency of the catheter length determined and then the QI calculated with regards to PTV_F. The distance between the catheter traces and possible changes in DNR yield information of possible modifications within the breast tissue and cold or hot spots within the dose distribution.

In case of alarming results, e.g., a drop of the CI under 90% or enlarged high dose regions, the cases were more detailed analyzed and discussed with experienced medical physicists and physicians, who finally decided if an adaption of the treatment plan was necessary.

Retrospective data analysis

In order to get quick and reliable results whether re-planning would be necessary based on parameters and not on expertise, the estimation scheme from clinical routine was extended by adapting the PTV structure based on the estimated CT deformations. The estimated deformed PTV is referred to as PTV_{DIR} in the following.

In a first estimation step, the defined catheter traces of PCT and FCT were both fitted with a third degree polynomial, sampled with a spacing of 0.2 mm, pre-aligned and following rigidly registered onto each other using a coherent point drift algorithm [17]. The discrete Fréchet distance (δ_F) [18] between the two curves was calculated in order to investigate the similarity between the defined catheter paths. The discrete Fréchet distance describes the maximal distance between two curves considering all vertices of the two polygonal curves and is defined according to Alt et al. [18] as the following:

$$\delta_F(P, Q) = inf\ max \| P(\alpha(t)) - Q(\beta(t)) \|$$

where P, Q are parametrizations of the two curves and α, β, $t \in [0, 1]$.

Further, the length between the catheters defined on PCT was compared to the length of the adapted catheter traces (ΔL), which

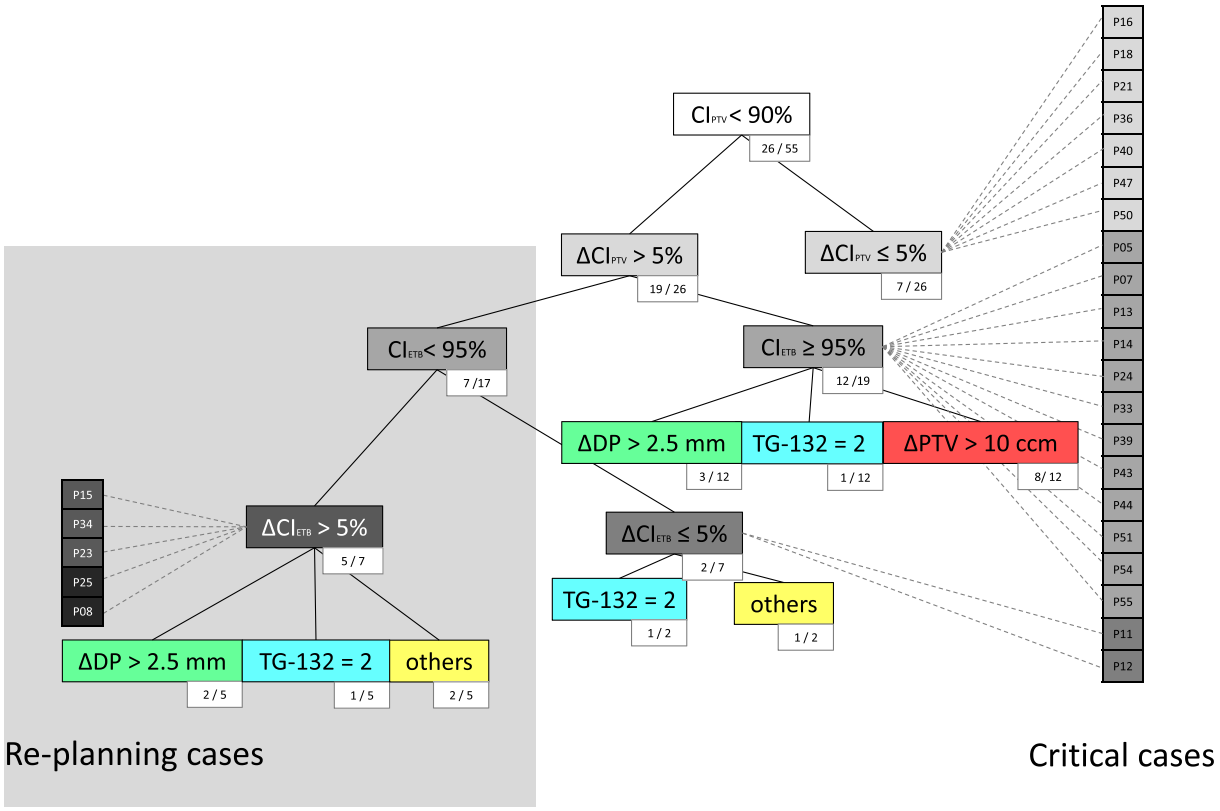

Figure 1. Decision tree for re-planning.
The figure shows the used schema to decide if re-planning is necessary. Pxx presents the patient identification number. On the right side the critical cases and on the left side the cases were re-planning would have been beneficial are listed. For each considered parameter the number of assigned patients is presented. All patients, where $\Delta CI_{PTV} > 5\%$ and $CI_{PTV} < 90\%$ were categorized according to possible reasons for the deviations, e.g. ΔPTV, ΔDP or DIR. The region underlay with gray marks the cases, which have to be carefully considered for re-planning. PTV = planning target volume; ETB = estimated tumor bed; CI_{PTV} = coverage index within PTV; CI_{ETB} = coverage index within ETB; TG-132 = quality of deformable image registration according to AAPM TG-132; ΔDP = dwell position deviation; ΔCI = difference between CI planning and estimated CI on follow-up CT; ΔPTV = difference of estimated PTV volumes.

were reconstructed based on FCT. The length of the catheters is defined as the linear connection of all defined catheter points starting and ending at the button centers. In addition, the Euclidean distance between the corresponding DPs was assessed and the mean deviation per catheter used for evaluation (ΔDP). Using principle component analysis the deviations were further divided into shifts in implant direction and in migrations in lateral direction. The magnitude of the shifts in implant direction was used to adapt the offset value within the TPS in order to simulate a shift back or forward of the catheter traces. This way the influence of ΔDP on the dose distribution could be verified. For the estimation of geometrical deviations an in-house MATLAB (Version *R2015b*, MathWorks, Massachusetts, USA) routine was used.

A multi-stage multi-resolution deformable image registration (DIR) was performed matching PCT to FCT using an in-house script implemented with the open source software plastimatch [19]. Prior DIR, the center of the images were aligned and a rigid image registration was acquired to roughly align the CT images. The quality of DIR was visually verified using a toolbox in Slicer3D [20] and the accuracy level was classified according to the AAPM Report TG-132 [21]. The estimated vector field was used to deform the PTV contour to account for possible changes within the breast tissue and to determine the best estimation of the follow-up PTV_{DIR} without re-contouring. The deformed structure was resampled onto FCT and imported into the TPS. And similar to the weekly quality assurance approach the QI were determined.

In order to estimate the need for adaptive planning various factors were taken into account considering the PTV_{DIR}: $CI_{PTV} < 90\%$; $\Delta CI_{PTV} > 5\%$; $CI_{ETB} < 95\%$ and $\Delta CI_{ETB} > 5\%$, where CI_{PTV} describes the coverage index of the PTV, CI_{ETB} stands for the coverage index of the estimated tumor bed (ETB) and ΔCI_{xx} defines the deviation of the coverage index to the treatment plan. Further, ΔDP greater than 2.5 mm, the order of the step size, indicates a migration of the catheter paths and ΔPTV greater than 10 ccm defines a change within the breast tissue, e.g., swelling. All defined thresholds are based on clinical expertise. Figure 1 summarizes the decision process, whether re-planning might be beneficial for the patients.

The correlation (ρ) between different variables, like patients' age, number of catheters, breast volume, PTV, ΔCI_{PTV}, δ_F or ΔL and ΔDP was evaluated using the Spearman-rank correlation with a confidence level of 0.95 implemented in R (R Foundation for Statistical Computing, version 3.3.2) [22].

Important parameters and variables used for the evaluation are summarized in Supplementary Table 1.

Results

On average ΔDP was determined to 2.41 ± 1.73 mm and ranged between 0.38 mm and 15.4 mm considering all estimated catheters. The mean standard deviation within one catheter was 0.18 ± 0.16 mm. Figure 2 summarizes all results considering the deviations between the treatment plan estimated on PCT and FCT. Dividing the deviations in their main components, a mean shift in implant direction was estimated of 1.54 ± 1.30 mm and a lateral migration on average of 1.59 ± 1.23 mm. A mean δ_F of 3.31 ± 2.04 mm (range 0.89–17.31 mm) was estimated between the reconstructed catheter paths. A minor correlation between ΔDP and δ_F could be proven ($\rho = 0.71$). In the mean the length of

the catheters varied 1.73 ± 3.12 mm and no correlation between increased ΔDP and Δ*L* or the catheter length could be shown.

Comparing the mean ΔDP for each patient a minimum of 0.97 mm and a maximum of 5.81 mm was yield. Figure 3 shows the exemplary results for patient P04, which had a mean ΔDP of 1.31 mm considering all 15 implanted catheters.

The mean variation in skin or ribs $D_{1.0ccm}$ ($\Delta D_{1.0ccm}$) comparing the exposure on FCT to PCT were determined to $\Delta D_{1.0ccm}$ (skin) = 5.37 ± 6.30% and $\Delta D_{1.0ccm}$ (ribs) = 4.62 ± 4.51 %. The changes of CI_{PTV} (ΔCI_{PTV}), DNR (ΔDNR) and COIN (ΔCOIN) estimated on PTV_F and the adapted catheter reconstruction were estimated to 3.10 ± 3.17%, 0.009 ± 0.007 and 0.036 ± 0.040, respectively. Two out of 55 cases (P34, P25) were classified in the weekly quality assurance routine as critical, however only one patient (P34) was re-planned.

Using the AAPM TG-132 evaluation scheme, 35% of the DIRs of PCT and FCT were classified as perfectly matched (TG-132 = 0), 49% as registration with minor changes, but locally aligned (TG-132 = 1), 16% with enlarged deviations (TG-132 = 2) and none of these registrations was erroneous or not suitable to identify the general area (TG-132 = 3, 4). The absolute PTV change (ΔPTV) was in the mean 6.65 ± 8.81 ccm after deformation and the absolute variation ranged between 0.21 ccm and 44.08 ccm. The CI_{PTV} of PTV_{DIR} differed in the mean 5.05 ± 4.14% from the calculated and planned CI_{PTV}. Figure 4 summarizes all results considering the dosimetric quality indices and the estimated deviations. Considering the deformed structures, in 26 of 55 cases the CI_{PTV} dropped below the recommended threshold. However, in only 19 of the 26 cases the ΔCI_{PTV} was larger than 5%. In 15 out of the 26 cases the rigid prediction confirmed the drop of the CI_{PTV}. Considering the exposure on the skin, only 11 of the 55 cases crossed the suggested boundary of 90% for $D_{1.0ccm}$, but only in 6 cases the change was higher than 5%. An increased skin dose was mostly connected to an enlarged ΔDP. Out of the 19 cases where CI_{PTV} <90% and ΔCI_{PTV} >5%, in 42% ΔPTV was greater than 10 ccm, in 16% the registration was not accurate, in 26% ΔDP was greater than 2.5 mm and in 16% no obvious reason for the deviation could be found. 5 cases out of 17 cases were considered to be critical, where CI_{ETB} <95% and ΔCI_{ETB} >5%. We found a change in PTV of more than 10 ccm in 8 of all 55 considered patients. In all of these patients the CI dropped below 90%, but the ETB was still sufficiently covered. However, in 2 out of these 5 cases (P15, P34) CI_{ETB} could be increased to more than 95% by simulating shifting the catheters in implant direction in the TPS. In one out of the 5 cases the registration was inaccurate, which has a strong impact on the precision and reliability of the prediction. Hence, re-planning would have been necessary for the remaining two cases.

The results show that in 2 of the 55 patients (P08, P25) re-planning should be considered, where the CI dropped below 90% and the deviation could not be resolved by shifting the catheters. In 3 of the 5 critical cases, which were considered as candidates for re-planning, the treatment plan assessed with PTV_F indicated similar results. 2 of the 5 cases (P34, P25) were identified as critical in the weekly quality assurance routine, however only one patient (P34) was re-planned. Conducting the decision tree based on PTV_F three cases (P13, P15, P23) were identified as critical, which are all connected to an enlarged ΔDP. The results of the decision tree, if re-planning is necessary, are presented in Figure 1, all detailed results are summarized in Supplementary Table 2 and visualized in Figure 4.

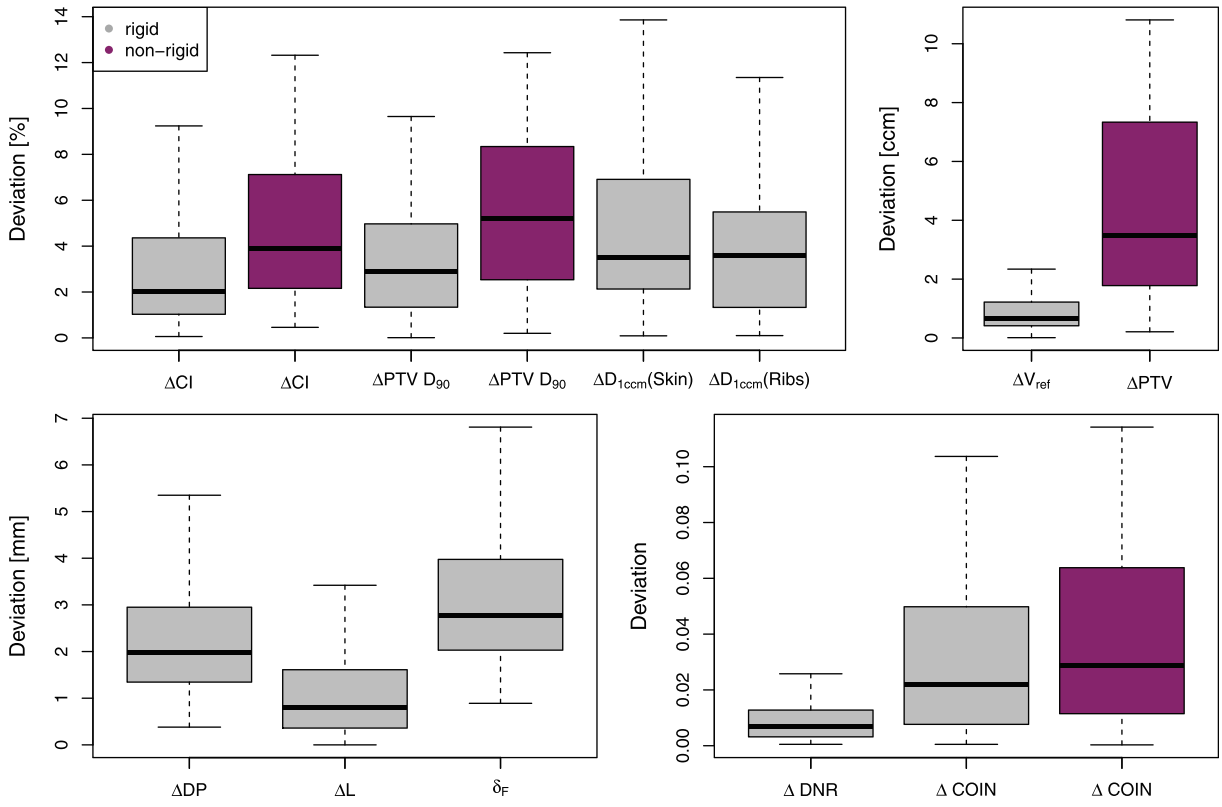

Figure 2. Summary of estimated deviations.
The subfigures show the calculated deviations to the treatment plan. In gray the results for the rigidly warped PTV structures are presented and in magenta the changes considering the deformed PTV. ΔCI = deviations of coverage index; ΔPTV D_{90} = difference of the average dose to 90% of the PTV; $\Delta D_{1.0ccm}$ OAR = deviation of exposure of OAR; ΔV_{ref} = change of volume encompassed by D_{ref}, ΔPTV = difference of the defined PTV and the deformed PTV; ΔDP = deviation of corresponding dwell positions; ΔL = change of the catheter length; δ_F = Fréchet distance between defined catheter traces; ΔDNR = deviation of the DNR; ΔCOIN = deviation of the calculated COIN. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

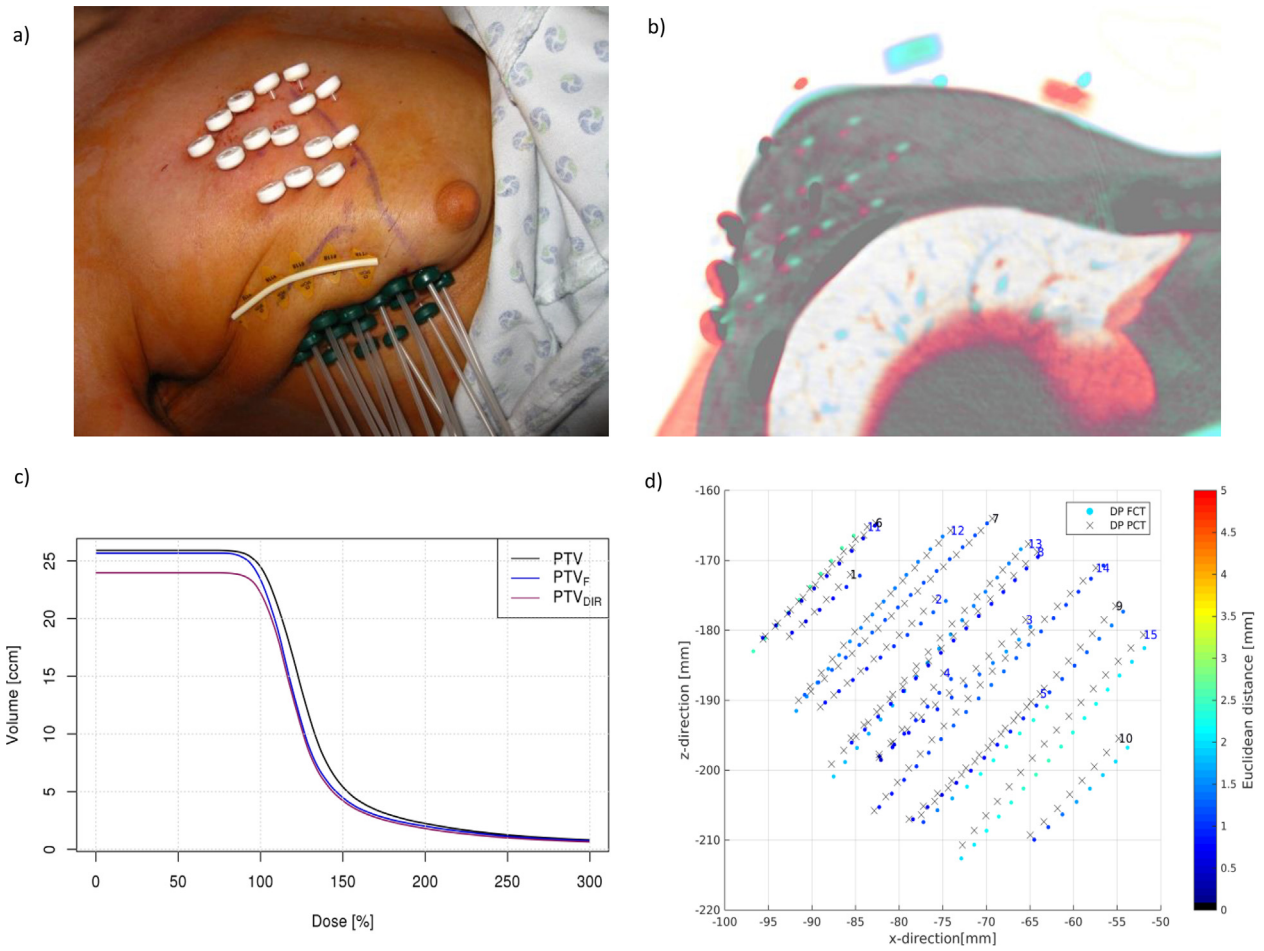

Figure 3. Exemplary results for patient P04.
Subfigure a) shows an image of the patients' breast after implantation. Subfigure b) presents the rigidly registered PCT and FCT. Subfigure c) represents the estimated DHVs for the planning dose distribution, the dose distribution evaluated with the rigidly warped PTV onto FCT (PTV_F) and the dose distribution after deforming the PTV structure (PTV_{DIR}). Subfigure d) shows the defined DPs in PCT and FCT and color coded with the estimated deviations. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Discussion

Various different influences could lead to a drop in CI and other quality indices and should be examined individually. A change in DNR, V_{ref} (Implant) or PTV could indicate migration of the catheters caused by swelling or shrinkage of the breast. Another cause of changes is the probability of catheter shifts in implant direction, which could have a strong impact on the dose distribution and especially on critical OARs like the skin [23]. The magnitude of migration seems to be similar in lateral direction as well as in implant direction, however in at least 5 of the 26 critical cases the CI could have been improved by simulating shifting the catheters back in implant direction, a process that can be easily done by the medical technical assistant prior each fraction if the shifts are reliably detected.

For our evaluation we classified ΔDP greater than the defined step size as critical, however it is difficult to define a general threshold upon which severe changes can be expected. The impact of shifts depends on the location of the catheter within the implant geometry and relative to the organs at risk. Also the amount of DPs within the catheter and the specific DT of the DPs have an influence. Moreover, the position of the implant geometry within the breast, e.g., close to the skin or ribs, influences the consequence of a shifted catheter. Nonetheless, shifts greater than the step size indicate changes such that the result has to be evaluated and the case analyzed in detail.

In patient P04 no reason for an increased exposure on the skin, like a large ΔDPs or ΔPTV, could be proven and the PTV was sufficiently covered, however an increased exposure of the skin was remarked, see Figure 4. Overall, it is difficult to decide, when re-planning is necessary. In our proposed decision tree we mainly concentrated on the coverage of the target volume, but also hot spots, parts of the volume that are dosed >100% of D_{ref} and the exposure of the OARs may play an important role. Further, the estimation of the deformation field and the additional catheter reconstruction might extent the clinical time capacity and feasibility of adaptive treatment planning, since until now no deformable image registration is incorporated into the TPS nor a fast automatic catheter reconstruction algorithm. The manual catheter reconstruction usually needs 3–5 minutes per catheter and is one of the most time consuming parts in treatment planning as well as contouring of the OARs. The time factor is at the moment one of the major limitations to incorporate adaptive treatment planning on a daily basis.

Considering the presented results, it is impossible to define one specific parameter to trigger re-planning. A precise analysis of CI, ΔDP, ΔPTV, ΔCOIN and ΔCI is necessary in order to get a meaningful prediction; Supplementary Figure 1 shows another extended approach to identify candidates for re-planning. The extended approach classifies critical cases before DIR is performed with regards to ΔDP, ΔDNR and takes into account the exposure on the OAR. Thus, in only 41% of the patients the effort of a DIR needed to be done and also the same two cases (P08, P25) for re-planning

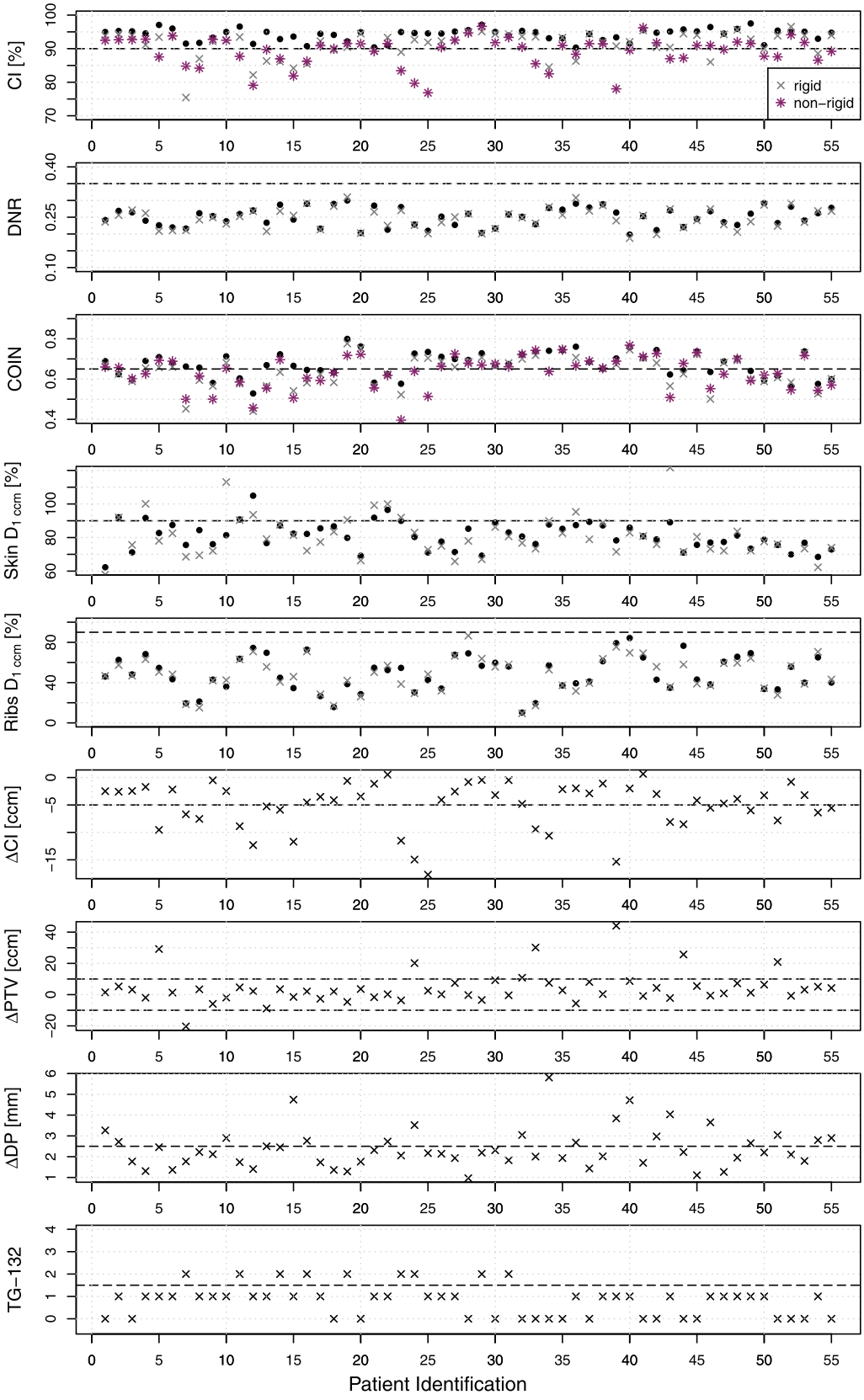

Figure 4. Deviations of the patient cohort.
For each patient the estimated values of the treatment plan are compared to the estimated value on the follow up CT with a rigidly warped PTV_F (cross) and the deformed PTV_{DIR} (star). The dashed line represents the recommended threshold for treatment planning and for evaluating the deviations. All deviations present the difference between the planning situation and the estimated treatment using PTV_{DIR}. ΔPTV = difference of the defined PTV from treatment planning and the deformed PTV_{DIR}; CI = coverage index; DNR = dose non-uniformity ratio; COIN = conformal index; $D_{1.0ccm}$ OAR = exposure of OAR; ΔDP = deviations between corresponding dwell positions; TG-132 = classification of deformable image registration according to AAPM TG-132.

were identified. A compromise between time effort, precision and reliability of the detection rate should be found and probably there is no simple explicit solution. Until now, despite the decision algorithm performed clinically after follow-up CT acquisition, the decision of re-planning was taken based on the expertise of the medical physicist and physician not according to a precise scoring system.

By changing the offset value within the TPS, we tried to simulate an actual shifting of the catheter. It was proven that in all critical cases connected to a large ΔDP the loss in CT_{ETB} could be compensated by shifting. In 36% of all patients a ΔDP greater than 2.5 mm, which is equivalent to the DP step size, was detected and could thus have been corrected by real-time quality assurance interventions prior irradiation, like electromagnetic tracking [24].

Within the presented patient cohort only the treatment plan of one patient was adapted (P34), because of large ΔDP (>5 mm). In this case an additional follow-up CT after the 6th fraction was acquired, a new target volume delineated and an adapted treatment plan established for the remaining fractions. With the new treatment plan the CI increased from 82.50% to 97.35%. Applying the adapted treatment plan onto the FCT with the corresponding catheter reconstruction and establishing the resulting quality indices, the CI was augmented to 88.15%. By shifting the catheter paths back in implant direction the CI on FCT was improved form 82.50 –87.75%.

The FCT is suitable not only for adaptive treatment planning but also serves as additional quality assurance to detect possible planning errors, by comparing, double-checking and analyzing the reconstructed catheter traces and the resulting dose distribution, to ensure the planned dose delivery, since in case of an error the plan could be adapted for the remaining fractions [25]. However, the time of acquisition after the 4th fraction is not ideal in case this reasoning have highest priority. The presented results are dependent on the quality of the registration. In three of the critical 19 cases the DIR was classified as imprecise (TG-132 = 2) and thus the estimated values are overlaid with this effect and no reason for large deviations could be identified. An imprecise registration will lead to an erroneous enlarged ΔDP and loss in CI. The quality of DIR suffers in case of difference in the reconstructed field of view of PCT and FCT. Also, the resampling of the PTV structure to the FCT implicates interpolation and thus uncertainties within the target structure and dose grid cannot be avoided [26]. Even with acquiring planning CT and follow-up CT using the same parameters difference in the reconstruction field size and the position of the breast are indispensable.

A drawback of the study is that the catheter reconstruction (mean DP deviation = 0.60 ± 0.35 mm) as well as contouring of the OARs is susceptible by inter-observer variations [27,28]. Thus, the estimated deviations are overlaid by these effects. Deforming the PTV according to the breast deformation seems to be a good approach in order to gain a better understanding of possible alterations. Especially, considering the large inter-observer variations for target delineation, the attempt presents the fastest procedure that allows estimation on whether or not re-planning is necessary. In case re-planning is necessary and a new treatment plan will be being established, a new PTV structure will be necessary in either case.

However, the acquired FCT is just another snapshot of the deformed breast and the applicator placement. Varying breast positions in time of irradiation, healing processes and migration of the applicator lead to deviations and have an effect on the breast tissue and consequently the PTV. In order to introduce a complete scheme for treatment plan adaption an investigation when the FCT should be acquired might be advisable. Another alternative for quality assurance in time of the therapy is the use of dose-free imaging modalities like ultrasound, magnetic resonance tomography (MRT) or tracking procedures e.g., electromagnetic tracking or optical tracking systems to gain a daily impression of the breast or the catheter traces [23,29–31].

Scanderbeg et al. [12] proved that after 24 h the tissue conformance is recuperated when using SAVI. Until now, it was never estimated if the tissue needs time for recuperation in iBT and if more time between implantation and acquiring the PCT might be beneficial to ensure the planned dose delivery.

In conclusion, a mean ΔDP was determined to 2.41 ± 1.73 mm considering all estimated catheters. Re-planning was suggested in 4% of the cases, where CI_{PTV} and CI_{ETB} dropped under 90% and 95 %, respectively. On average CI_{PTV} differed 5.05 ± 4.14% from the calculated and planned CI considering PTV_{DIR}. The presented results show that adapting the distance of the first DPs, defined as offset in the treatment plan, seems to be beneficial for 35% of the patients to ensure the planned dose delivery. This way shifts in implant direction could be easily compensated on a daily basis. However, treatment verification and adaption is time consuming and a dose-free automatic fast estimation scheme should be introduced.

In summary, we can conclude that it is especially important to maintain the planning situation and account for occurring changes within the implant, since deviations over the week of treatment could be proven. However up to this point, we are only able to quantify and report occurring deviations. In order to assess the consequences of the changes in e.g., CI, the results have to be combined with long-term follow-up data to create overall guidelines.

The proposed estimation scheme showed that it is tricky but feasible to establish a scoring system or guidelines considering ΔDP, ΔPTV, ΔCI and CI to trigger re-planning. Further, our method could be used as means and first step to standardize and introduce protocols regarding the classification of critical cases, where re-planning should be carried out, as until now, re-planning is done based on the expertise not according to a precise scoring system. Nonetheless our exemplary thresholds are not universally valid and only prove the concept of the possibility and necessity for such a scoring system for adaptive treatment planning.

Declaration of Competing Interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2019.08.015.

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