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Original Article

Auto-planning for VMAT accelerated partial breast irradiation

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ABSTRACT

Purpose: To evaluate the quality of accelerated partial breast irradiation (APBI) plans generated by the Auto-Planning module of a commercial treatment planning system (TPS).
Material and methods: Twenty patients, previously planned and treated with manual planning in a TPS (manM), were re-planned using manual (manP) and automatic (AP) module of a different TPS. Plans were compared in terms of dosimetric parameters, degree of modulation, monitor units and treatment time, and by blind qualitative scoring by a physician. Dosimetric verification was evaluated in terms of γ passing rate and point dose measurements. Statistical differences were evaluated using paired two-sided Wilcoxon's signed-rank test.
Results: A statistically significant improvement in PTV coverage was observed for AP plans compared to clinical plans, while no differences in organs at risk doses were observed. When compared to manP plans, a statistically significant improvement was observed for PTV coverage and homogeneity and for the ipsilateral breast and lung dosimetric parameters. The modulation degree was reduced with AP compared to manM treatment plans, while it was increased compared to manP treatment plans. No differences were observed in γ passing rate. Planning time was reduced from (54.5 ± 8.0) min for manM planning and (62.8 ± 15.0) min for manP planning to (9.8 ± 1.1) min for AP. In the qualitative scoring, AP plans were considered superior both to manM (10/20 cases) and manP plans (12/20 cases) with high clinical relevance.
Conclusion: Automatic planning for VMAT APBI was always at least equivalent and overall superior to manual planning.

Plan optimization as performed in IMRT (Intensity Modulated Radiation Therapy) and VMAT (Volumetric Modulated Arc Therapy) treatment planning is a highly complex and time-consuming process, involving many manual steps. The choice of the planning objectives and constraints depends on the specific clinical situation, patient anatomy and target location and the final result is considerably influenced by planner experience.

Additional help structures are frequently introduced to refine the dose distribution. Since individual planners construct their individual help structures in different ways, this could further impair the reproducibility and consistency of the plan generation process. The final plan quality is broadly variable and it is also dependent on the available planning time. For these reasons and for the required frequent manual interaction between planner and treatment planning system (TPS), IMRT and VMAT treatment planning represents a huge workload for radiotherapy departments [1,2]. Standardization in radiotherapy treatment planning is important in order to guarantee to all patients a high quality treatment independently of the planner time and skills. Currently, even within the same clinical planning protocol, a large variation in planning solutions may be proposed by different planners [3–6].

Automatic planning has been recently introduced [7–10] with the aim of reducing planning time and inter-operator variability. It can be implemented in TPS using different algorithms, the most common methods being the knowledge-based and the planning simulation approaches. The first approach uses past treatment plans to predict DVH for a new patient, as in Varian's RapidPlan module (Varian Medical System, Palo Alto, CA) [7]. In the second approach an iterative optimization method is used to mimic the planning process with an iterative reduction of cold and hot spots, as in the Auto-Planning module of Pinnacle[3] TPS (Philips Radiation Oncology Systems, Fitchburg, WI) [8]. In addition, iCycle algorithm is another automated plan optimization method based on a wish list established from iterative planning and plan evaluation [10]. Many studies have shown that an automatic approach can improve both planning efficiency and plan quality consistency [6,11,12], but

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a careful validation of automatically generated plans is required. The validation aims at determining whether (and where) an advantage exists in the automatic approach when compared to manual planning and should consist in the comparison between automatically generated plans and manually generated clinical plans, which still represent the gold standard [11,12].

Accelerated partial breast irradiation (APBI) is part of our clinical practice, and it is widely adopted in our center for selected low risk breast cancer patient.

The aim of the current study is to provide an approach for protocols' validation, a way of creating treatment technique for APBI and a practical tool for those who want to implement APBI automatic planning in the clinical routine.

Therefore, we evaluated the Auto-Planning (AP) module of the Pinnacle^3 (Philips Medical Systems, Fitchburg, WI) TPS in a cohort of APBI patients. Validation was conducted by comparing automatically generated VMAT plans with clinically accepted VMAT plans generated with Monaco (Elekta AB, Stockholm, Sweden) and with manually generated Pinnacle plans. The arm of the clinical manual plans (manM) represents the gold standard, since it is composed by the plans that were clinically approved and used to treat the patients. The manual Pinnacle plans (manP) were useful to understand whether advantages in AP are actually due to automation or to the different optimization engines.

Materials and methods

Patients and clinical planning

Thirty left-sided breast cancer patients were selected for this study. All of them were planned for APBI using 6 MV photon beams from an Elekta Synergy linac (Elekta AB, Stockholm, Sweden) equipped with a Beam Modulator multileaf collimator. All plans were generated with conventional manual planning, using the Monaco TPS (version 5.10), which is the TPS clinically employed in our center for APBI VMAT plans.

For each VMAT plan a partial arc was used with start and stop angles specific for each patient in order to better spare organs at risk (OARs): heart, ipsilateral lung and contralateral breast. Different arc amplitudes are generally used for different anatomies and quadrant location.

The clinical target volume (CTV) was delineated with a uniform 1-cm three-dimensional margin around the surgical clips. A second uniform, three-dimensional 1-cm margin was added to the CTV to obtain the planning target volume (PTV). The PTV was allowed to extend maximum 4 mm inside the ipsilateral lung and was cropped 3 mm inside the patient's surface.

The ipsilateral and contralateral breast, ipsilateral and contralateral lung, heart, and spinal cord were contoured as OARs. A dose of 30 Gy in 5 fractions was prescribed.

The following constraints were adopted for plan optimization, as previously published [13]:

PTV: $V_{28.5\ Gy} \geq 95\%$, $D_{max} \leq 110\%$ (33 Gy)
Ipsilateral breast: $V_{15\ Gy} \leq 50\%$
Ipsilateral lung: $V_{10\ Gy} \leq 20\%$
Contralateral lung: $V_{5\ Gy} \leq 10\%$
Contralateral breast: $D_{max} \leq 1$ Gy
Heart: $V_{3\ Gy} \leq 10\%$

All clinical VMAT plans were created by the same experienced medical physicist. The planner introduced no help structures during the manual planning process. Sometimes it was not possible to respect the ideal constraint for at least one OAR or for PTV in the manual clinical plan. In these cases, the patient was considered having an unfavorable or challenging anatomy. For these patients, a minor deviation from the ideal constraints was accepted by the approving physician.

Auto-planning module

AP automates the consecutive multiple sequence optimization process using a progressive optimization algorithm. Each plan is composed of 6 subsequent optimization cycles, with a user-definable maximum number of iteration per cycle. The number of optimization cycles is set by the vendor (not editable by the user); the constraints are automatically adapted after each cycle.

The AP module requires beam parameters and optimization goals to be set in the so-called Treatment Technique. The first 10 patients of the sample were used to establish and validate the Treatment Technique by varying the parameters that can be set by the user for determining their better combination. Those parameters are: the tuning balance, which enables the user to tune the weighting between target coverage and OARs sparing, the hot-spot maximum goal, the dose fall-off margin (expressed in cm and affecting conformity), the choice to use cold-spot ROIs for improving coverage and the clinical objectives with their priorities. Other parameters are the Constrain leaf motion, expressed in cm/degree, which depends on delivery machine characteristics and may affect the quality and accuracy of the dose distribution, and the number of control points/degree, also potentially affecting the agreement between calculated and delivered dose distributions.

Automated vs. manual planning – plan quality and planning time

Twenty patients, who had previously been planned with Monaco, were then re-planned using both manual Pinnacle (manP) and AP module with the established technique and with no further manual intervention. Pinnacle manual plans were performed in order to evaluate whether differences between AP and manual clinical plans are due to automation or to the different optimization engines of the two TPS.

For the manP plans and the AP plans, the same geometry (arc amplitude, start and stop gantry position) as in manual Monaco plans was maintained. For each patient, the AP and manual plans were compared by assessing differences in PTV $V_{95\%}$, $D_{1\ cc}$, $V_{105\%}$, heart $V_{3\ Gy}$, ipsilateral breast $V_{15\ Gy}$, ipsilateral lung $V_{10\ Gy}$, contralateral lung $V_{5\ Gy}$, contralateral breast $D_{1\ cc}$. In order to overcome the dose calculation differences between the implemented calculation algorithms in Pinnacle and Monaco, the two Pinnacle plans were exported to Monaco for dose recalculation. Recalculated plans were then used to derive all the dosimetric parameters.

For each patient, the AP and manual dose distributions were also independently evaluated and blindly compared by an experienced clinician. For plan scoring, a cross was drawn on a visual analog scale as proposed in the work by Heijmen et al. [14]. Planning time was measured for both manual and automatic approach. Planning time was defined as the effective working time required, while the time required for the optimization was not measured since it strongly depends on the hardware characteristics.

Automated vs. manual planning – modulation degree, total MU and delivery time

Apart from the dosimetric quality, AP and manual plans were also compared in terms of degree of modulation, total number of MU and delivery time. The degree of modulation was evaluated through the Modulation Complexity Score (MCS) as defined in the work by Masi et al. [15]. Due to its mathematical formulation, the MCS has values in the range from 0 to 1. MCS = 1 means no modulation, and can be exemplified by an arc with a fixed rectangular aperture with no leaves moving during the arc. As modulation increases, MCS decreases.

Automated vs. manual planning – dosimetric verification

In order to check that both manual and AP plans could be reliably delivered, dosimetric verification was performed and evaluated in terms of γ passing rate (3%, 3 mm, local approach) and point dose measurements.

Each patient plan was transferred to the ArcCheck® (Sun Nuclear Corporation, Melbourne, FL) 3D array, using the quality assurance (QA) feature of each TPS. Additionally, point dose measurement was performed with an Exradin A1SL ionization chamber (Standard Imaging, Middleton, WI) placed in the detector center.

Statistics

Statistical significance of differences between AP and manual plans in dosimetric plan parameters, degree of modulation, MU, treatment time, γ passing rate and point dose difference was evaluated using paired two-sided Wilcoxon's signed-rank tests with a significance level of 0.05. All statistical analyses were performed with OriginPro (version 9.0.0, OriginLab Corporation, Northampton, MA).

Results

Patients and clinical planning

The mean PTV in the patients sample used for AP evaluation is (164 ± 61) cc (range 86–298 cc). The mean ipsilateral breast volume (IBV) is (818 ± 531) cc (range 177–2206 cc). The mean PTV/IBV is (26 ± 11)% with a wide range of variability (8–48%). Treated breast index quadrants were: upper outer (n = 9), lower outer (n = 4), central portion (n = 3), lower inner (n = 3), and upper inner (n = 1). Half of the patients of the selected sample (10/20) were considered having an unfavorable anatomy.

Auto-planning module

OARs' optimization goals used in the Treatment Technique are reported in Table 1. As a result of the optimization of the treatment technique, we set: the tuning balance to 11%, the dose fall-off margin to 2.6 cm, the hot-spot maximum goal to 105% and the "Use Cold-Spot ROIs" option checked. The maximum number of iterations was set to 60.

Automated vs. manual planning – plan quality and planning time

Dosimetric parameters for manual (manM and manP) and AP plans are reported in Table 2. A statistically significant improvement in PTV coverage (average 0.6%; range -0.9–5.9%) was observed for AP plans compared to manM plans. Although not statistically significant, an improvement in PTV dose homogeneity (3% average reduction in PTV $V_{105\%}$) was observed for AP plans compared to manM plans.

No statistically significant differences in OARs doses were found, although a trend in the reduction in ipsilateral breast $V_{15\ Gy}$ (considered clinically significant by the scoring physicians) was observed (average reduction in $V_{15\ Gy}$ 0.4%).

When compared to manP plans, advantages of automatic planning were more evident: a statistically significant improvement was observed in PTV coverage (average 3.0%; range −0.4%–6.4%) and PTV dose homogeneity (9.1% average reduction in PTV $V_{105\%}$). Statistically significant reductions in ipsilateral breast $V_{15\ Gy}$ (average 2.1%) and ipsilateral lung $V_{10\ Gy}$ (average 4.6%) were observed.

In 6 out of 10 patients having an unfavorable anatomy (for whom a minor deviation from the ideal constraint was accepted in the manual clinical plan) the deviation was solved by the AP, while in remaining 4 cases it was anyway reduced with respect to the manual plan.

In Fig. 1 (man M) and Fig. 2 (manP) the histograms representing the distribution of the differences between manual plans and AP are reported for all dosimetric parameters.

In the blind scoring performed by the physician, for 10/20 plan comparisons the AP plan was considered superior to the manM plan, with some possible clinical relevance. In 8/20 the AP plan was considered better but with no clinical relevance, while in 2/20 the plans were considered to be equivalent. Compared to manP plans, the AP plan was considered always superior, in 12/20 cases with some possible clinical relevance, while in 8/20 with no clinical relevance.

Concerning planning times, 9.8 min ± 1.1 min ranging from 5.8 to 12.5 min were required for AP compared to 54.5 min ± 8.0 min for the manM plans ranging from 48.0 to 65.5 min and to 62.8 min ± 12.0 min for the manP plans ranging from 49.5 to 68.0 min.

In Fig. 3 the dose distribution for manual Pinnacle plan, manual Monaco plan and AP together with the comparison between the three DVHs is reported for a representative patient.

Automated vs. manual planning – modulation degree, total MU and delivery time

Overall, the modulation degree was reduced with AP compared to manual Monaco plans (MCS in Monaco plans is 25% lower compared to AP plans). MUs and treatment time were also reduced: manM plans have on average 29% more MUs and last on average 8.4 s more than AP plans.

ManP plans are the one with the lowest modulation (MCS 20% lower on average than AP plans), the lowest number of MUs (on average 18% less than AP plans) and consequently with the lowest duration (an average 69 s less than AP plans). Data are summarized in Table 2.

Automated vs. manual planning – dosimetric verification

No statistically significant differences were observed in γ passing rates, which were on average ≥96% for the three planning methods. The agreement between point dose measurements and calculated dose was always very good (below 1.5%) with a better agreement for Pinnacle plans compared to Monaco (Table 2).

Table 1
OARs optimization goals in the Treatment Technique.

OAR	Optimization goal	Priority
Heart	$V_{3\ Gy}$ <10%	High
Ipsilateral breast	$V_{15\ Gy}$ <50%	High
Ipsilateral lung	$V_{10\ Gy}$ <20%	High
	D_{mean} <6 Gy	High
Contralateral lung	$V_{5\ Gy}$ <10%	High
	D_{mean} <2 Gy	High
Contralateral breast	D_{max} <1 Gy	Medium

Discussion

External beams partial breast irradiation for well-selected patients is widely increasing, due to promising results of several phase 3 trials [13,16–18]. Concerns still remain about the best technique and fractionation choice: main open points are related to the ideal recovery time between fractions (in the case of a daily bi-fractionation), and to the total dose to the ipsilateral healthy breast [19]. Moreover, target delineation is still a challenge [20], and the cooperation among several involved professionals

Table 2
Plan parameters for manually generated plans with Pinnacle (manP) and Monaco (manM) and automatically generated plans (AP). *p*-values are for the comparison between manual and automatic.

	Parameter		Mean value ± 1 SD	Range	*p*-value
PTV	$V_{95\%}$ [%]	manP	94.7 ± 1.8	90.6–97.3	<0.001
		manM	97.0 ± 2.0	91.1–99.0	0.02
		AP	97.6 ± 1.8	94.7–100.0	–
	$D_{1\ cc}$ [Gy]	manP	32.2 ± 0.4	31.1–33.1	0.002
		manM	31.8 ± 0.6	31.2–34.0	0.49
		AP	31.7 ± 0.4	30.8–32.3	–
	$V_{105\%}$ [%]	manP	13.1 ± 8.9	1.6–28.8	<0.001
		manM	6.9 ± 7.8	0.0–27.2	0.27
		AP	3.9 ± 3.3	0.0–8.0	–
Heart	$V_{3\ Gy}$ [%]	manP	7.5 ± 3.7	0.0–12.7	0.28
		manM	5.7 ± 3.7	0.0–12.4	0.38
		AP	6.7 ± 4.7	0.0–13.6	–
Ipsilateral breast	$V_{15\ Gy}$ [%]	manP	43.8 ± 11.3	17.4–55.8	<0.001
		manM	42.1 ± 13.4	16.9–61.9	0.70
		AP	41.7 ± 11.2	16.7–52.8	–
Ipsilateral lung	$V_{10\ Gy}$ [%]	manP	18.4 ± 6.4	0.0–34.3	<0.001
		manM	13.1 ± 5.1	0.1–20.0	0.34
		AP	13.9 ± 5.9	0.0–22.4	–
Contralateral lung	$V_{5\ Gy}$ [%]	manP	0.1 ± 0.5	0.0–2.1	0.27
		manM	0.6 ± 1.7	0.0–7.6	0.56
		AP	0.4 ± 0.8	0.0–2.5	–
Contralateral breast	$D_{1\ cc}$ [Gy]	manP	0.9 ± 0.3	0.5–1.7	0.06
		manM	1.2 ± 0.4	0.6–2.3	<0.001
		AP	1.0 ± 0.4	0.6–2.1	–
Treatment complexity	MCS	manP	0.49 ± 0.07	0.32–0.62	<0.001
		manM	0.31 ± 0.07	0.22–0.52	<0.001
		AP	0.41 ± 0.05	0.32–0.50	–
Treatment MU and duration	Treatment time [s]	manP	114 ± 17	84–162	<0.001
		manM	190 ± 23	144–240	0.18
		AP	182 ± 7	168–193	–
	MU	manP	744.4 ± 112.2	578.8–1090.0	<0.001
		manM	1175.4 ± 158.5	867.5–1491.9	<0.001
		AP	911.8 ± 78.7	814.0–1120.1	–
Dosimetric parameters	γ passing rate [%]	manP	96.0 ± 2.6	90.2–99.4	0.89
		manM	96.7 ± 1.5	93.5–98.4	0.40
		AP	96.4 ± 1.7	93.1–99.2	–
	Δ point dose [%]	manP	0.1 ± 0.7	−1.0–2.2	<0.001
		manM	-1.2 ± 1.3	−3.8–0.5	<0.001
		AP	0.8 ± 0.9	−0.1–3.6	–

(radiologists, breast surgeons, pathologists, radiation/clinical oncologists, physicists) seems to represent a crucial point for ensuring optimal targeted treatment in the era of breast conservation.

Many published papers investigated the comparison among different external beams partial breast irradiation techniques [21,22]. In particular, Essers et al. [23] demonstrated that VMAT is a good technique for APBI, improving PTV dose conformity and delivering lower doses to the ipsilateral breast and lung compared to 3D conformal radiotherapy (3DCRT), at the cost of a slight but acceptable increase in the contralateral breast dose. Moreover VMAT was shown to reduce cardiac dose if mean heart dose exceeds 0.5 Gy for 3DCRT.

There are no published experiences on automated planning approaches for APBI. Some peer-reviewed papers have compared (semi or fully) automated and manual planning for whole breast IMRT [24–28]. In all these studies, the described automated planning was, at least in part, based on in-house software or scripting, coupled with or integrated in commercial TPS. In all these studies, automatically generated treatment plans were clinically acceptable and often clinically improved or equal to the corresponding clinical plan. Moreover, important reductions in planning time were observed with respect to manual planning.

Several experiences have been recently published showing possible benefit deriving from the implementation of Pinnacle[3] AP in clinical practice [11,29–35] but, to our knowledge, this study provides the first results comparing manual planning to AP for external APBI. Although there are no strong theoretical reasons suggesting that automatic planning for ABPI may be very different than for other sites, we think that each anatomical site has its own peculiarities, thus making a specific validation of automatic planning for that application worthwhile. Published experiences so far were on head and neck [11,29–31], whole brain with hippocampal sparing [32], prostate cancer [33], spinal metastases [34] and liver stereotactic body radiation therapy [35]. A common conclusion is a significant reduction in dose to OARs in favor of AP. Overall, when a blinded clinical evaluation of the plans was accomplished, AP was shown to perform mostly better than or to be at least equivalent to the clinical plans [11,29,31,34,35]. Most of the automatically generated plans could potentially be used clinically without further optimization and automatic planning was also shown to improve homogeneity of plan quality with less dependence on anatomic complexity [11,12,14,24,25,33,36].

Moreover, an effective working time reduction in favor of AP was reported [11,35].

In our study we compared automatically generated plans with both manual clinical plans (generated with a different TPS, but considered the reference plans, since they were used to treat the patient) and manual Pinnacle plans, for investigating whether the

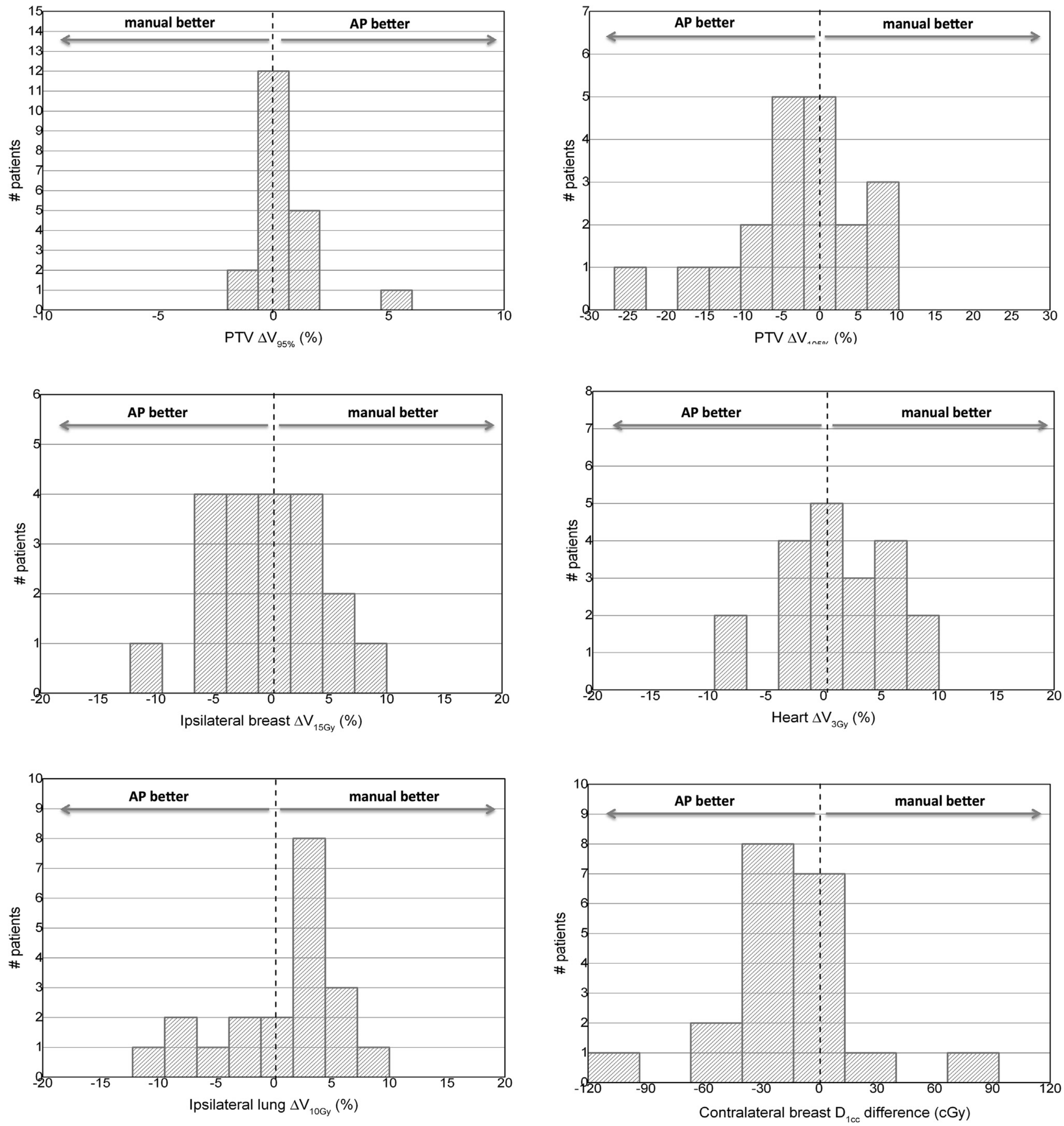

Fig. 1. Histograms of the differences between manual Monaco plans and AP plans for the investigated dosimetric plan parameters.

advantages in AP are actually due to automation or to the different optimization engines.

We observed a statistically significant improvement in PTV coverage with AP compared to clinical manual plans and no significant differences in OARs doses. A trend in the reduction in ipsilateral breast $V_{15\ Gy}$ was also observed. This is not negligible since ipsilateral breast dose–volume seems to be crucial in APBI toxicity outcomes [19]. In the blind scoring by the physician, 90% of AP plans were considered superior to the manual plans, in 50% of the cases with some possible clinical relevance, while 10% of the plans were considered to be equivalent.

When compared to manP plans, advantages of automatic planning were even more evident: a statistically significant improvement was observed in PTV coverage and homogeneity and for the ipsilateral breast and ipsilateral lung dosimetric parameters. In the blind scoring by the physician, compared to manP plans, the AP plan was considered always superior, in 60% of the cases with some possible clinical relevance. This could depend on the lower experience of the planners in using Pinnacle compared to Monaco for APBI, since all the clinical planning for APBI was done (before the introduction of AP) with Monaco. Considering that the role of Pinnacle manual plans is to improve the methodological

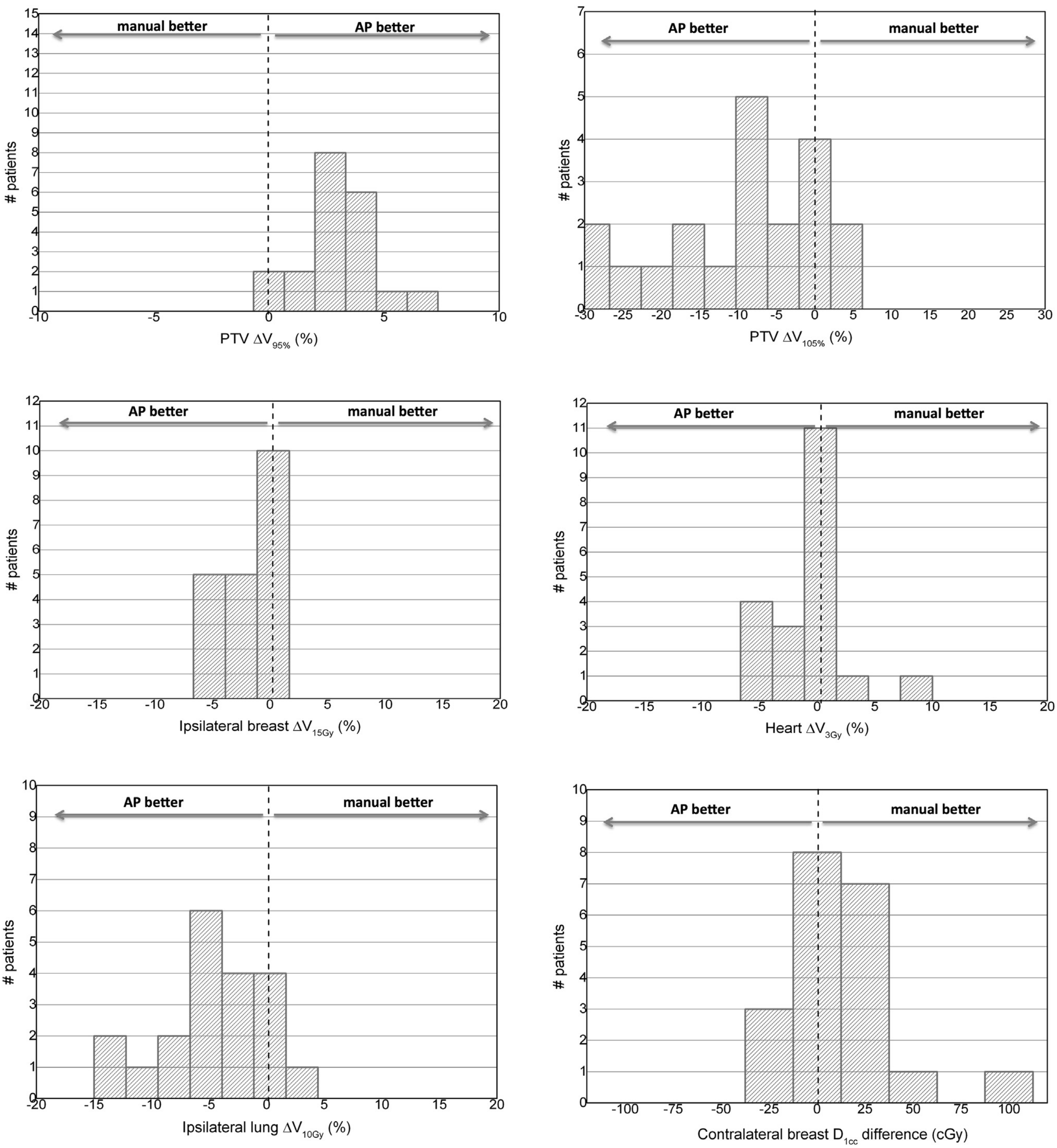

Fig. 2. Histograms of the differences between manual Pinnacle plans and AP plans for the investigated dosimetric plan parameters.

consistency of our work, rather than produce the best manual plans, we think that the lower plan quality we obtained with Pinnacle manual is not changing the main findings of our study.

A (practically unavoidable) limitation of the study, common to all the plan comparison studies involving manual planning, is that plan comparison is not bias-free, since the skills and experience of the planner influence plan quality.

Concerning standardization of plan quality, a reduction in plan variability is generally observed also in our cohort of patients, as can be seen looking at the ranges reported in Table 2.

ManP plans are the one with the lowest modulation, the lowest number of MUs and consequently with the lowest duration, while manM plans are the more modulated with highest MUs and duration. This suggests that the differences in terms of MU and degree of modulation between manM and AP can be mainly ascribed to the differences between the two TPS (different segmentation or cost functions) than to the use of automation.

In our study dose verification was also performed with the aim of checking that manual and AP calculated dose distributions could be reliably delivered and not with the aim of comparing them, since the observed differences in the dosimetric parameters (γ passing rates and point dose measurements) are far more dependent on the different TPS used, their calculation algorithm and beam fitting.

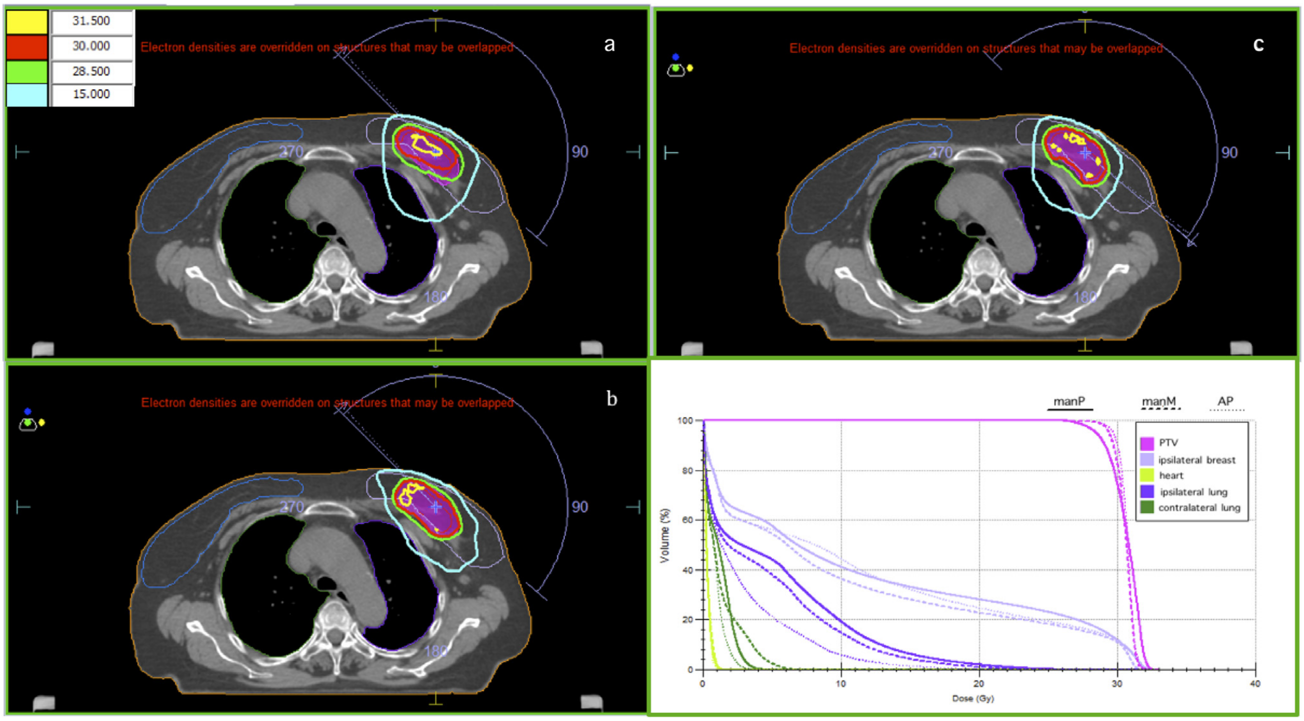

Fig. 3. Dose distribution for manual Pinnacle plan (a), manual Monaco plan (b) and AP (c) and comparison between the three DVHs (d).

In conclusion, our results show that overall plan quality and dose homogeneity in APBI AP plans was improved compared to manually generated plans. Automated treatment planning simplifies the plan optimization process while enhancing plan consistency, therefore reducing time and resources needed for treatment planning.

Conflicts of interest

None.

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