

The importance of the implant quality in APBI – Gliwice experience. Dosimetric evaluation

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Abstract

This study includes four years of our clinical trials to improve implant quality in multicatheter accelerated partial breast irradiation (APBI). The progress in dosimetric and volumetric parameters of the treatment plans was evaluated. One hundred and ninety-one women, for whom treatment plans were made based on three dimensional imaging, were selected for the study. To evaluate progress made in our APBI procedure, following parameters and indices were taken into account: percentage of the target volume receiving the reference dose (PTV_{ref}), minimum dose in the target volume expressed as a percentage of reference dose (PTV_{min}), dose homogeneity index (DHI), and conformity index (COIN). Additionally, the plan quality index was calculated for every group as the sum of mean values of four evaluated parameters. PTV_{ref} have increased from the mean value of 83.4% at the beginning to recent 94.8%. The maximum value equals to 95.4%. The same trend can be observed with PTV_{min} value, which has been improved from 51.7% to 70.1%, maximally. DHI and COIN mean values present similar progress. DHI value increased from 0.53 level to 0.68, and COIN from 0.58 in 2009 to 0.74. Plan quality index has increased from 2.46 in 2009 to 3.06, recently. The implant quality is crucial for the accurate dose distribution. This paper shows the progress that was made in APBI procedure to improve implant quality. Nowadays, our implant technique is based on three-dimensional CT imaging results in acceptable dose distributions.

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Purpose

The role of accelerated partial breast irradiation (APBI) for patients with early stage breast cancer has gained popularity as an alternative to the conventional whole breast irradiation (WBI) with external beam radiation [1-12]. In recent years, new single-entry breast brachytherapy devices have emerged offering simpler usage both for a patient and a physician [1,13]. However, multicatheter interstitial brachytherapy with flexible catheters located around the lumpectomy cavity, as the oldest one, has the longest experience. There are many studies presenting multicatheter interstitial APBI results in literature [1-14].

Because of the growing interest in APBI methods, guidelines and recommendations have been recently formulated [3]. In 2009, the American Society for Radiation Oncology (ASTRO) has published their statement on the use of APBI [15]. In the same year, the Groupe Européen de Curiethérapie European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) Breast Cancer Working Group has published the European guidelines for patient selection for APBI with interstitial brachytherapy (BT) [16].

In the past, two-dimensional radiography based imaging techniques were used in order to evaluate the dose distribution. However, in multicatheter APBI, the precise target definition and implant quality are crucial for accurate and conformal delivery of the prescribed dose to the planning target volume (PTV) with simultaneous sparing of normal tissue and organs at risk [2,7,8,11,17,18]. Three-dimensional imaging is therefore essential [3,18-22].

Since 2006, APBI as an adjuvant technique after breast conserving surgery has been used in Brachytherapy Department in Gliwice. From the beginning till the end of 2008, fluoroscopic films (two-dimensional, 2D imaging) were taken for both treatment planning and pre-planning procedures. Pre-planning was used to evaluate the implant geometry with respect to the target. The two-dimensional X-ray imaging system IBU-D (Integrated Brachytherapy Unit by Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) was used. Two orthogonal films were taken before insertion of needles to evaluate the location of the surgical clips, and after the implantation procedure to assess the geometric quality of the implant. Treatment planning, based on orthogonal films was per-

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formed with PLATO BPS v.14.3.3 planning system (Nucletron).

In 2009, three-dimensional computed tomography (CT) based treatment planning was introduced to APBI method. Treatment plans based on CT scans were created in the Oncentra MasterPlan v.3.1 planning system (Nucletron). The possibility of target delineating and estimating the target coverage with prescribed dose, as well as evaluating the maximum dose in organs at risk appeared.

This study covers four years of our clinical trials with multicatheter APBI based on three dimensional imaging. Dosimetric and volumetric parameters of the treatment plans were evaluated.

Material and methods

Between June 2006 and December 2012, 232 patients were treated with multicatheter APBI at the Brachytherapy Department in Memorial Cancer Center – Institute in Gliwice. One hundred and ninety-one of them, for whom treatment plans were made based on three dimensional imaging, were selected for the study. Since January 2009 till December 2012, eight separated groups have been created – one group every six months. We have used this approach to study the systematic improvement of the APBI technique with respect to the dosimetric parameters of the treatment plans.

All patients underwent breast conserving surgery. The cavity wall, after lumpectomy, was marked with the surgical titanium clips. The flexible catheters were implanted into the breast through a template, in a triangular pattern. Inter-catheter distance, number of planes, and catheters were adjusted with respect to the size and location of the target defined as a marked lesion with 0.5-2 cm margins. In the analyzed treatment plans, two or three-plane implants were used for all patients with 1.0-1.6 cm separation between the catheters.

Three-dimensional pre-planning method was performed with the Simulix Evolution Simulator (Nucletron). We have been trying to focus on pre-planning procedure emphatically all the time, as we consider it underlies as

the acceptable treatment plan. At the beginning of our trials with three-dimensional pre-planning, we performed cone beam CT acquisition to evaluate the surgical clips location. Then we decided to perform the second acquisition after inserting one plane of the needles to evaluate the position of the needles in relation to the marked lesion. Additional needles were inserted if necessary. In some cases, we decided to perform one more acquisition to make sure the needles positions were correct. Finally, the flexible plastic catheters were implanted into the breast to replace metal needles. Immediately after the implantation, computed tomography with Somatom Sensation Open 20 (Siemens AG, Munich, Germany) was performed for treatment planning purpose (catheter reconstruction, definition of planning target volume, and organs at risk volumes and plan evaluation). Treatment scheme was the same for every patient. The delivered dose was 32 Gy in eight fractions (4 Gy per fraction).

Treatment plans in each group were evaluated based on the dosimetric and volumetric parameters derived from the cumulative dose volume histograms (cDVH). Percentage of the target volume receiving the reference dose (PTV_{ref}), minimum dose in the target volume expressed as a percentage of reference dose (PTV_{min}), dose homogeneity index (DHI), and conformity index (COIN) has been selected for analysis. According to the definition of $DHI = 1 - (V_{150}/V_{ref})$, V_{ref} and V_{150} quantify volumes receiving the reference, and 1.5 times of the reference dose, respectively. The COIN determines coverage of the target by the reference isodose, including unwanted irradiation of normal tissues and is defined as $COIN = (PTV_{100}/V_{ref})(PTV_{100}/V_{PTV})$. PTV_{100} is the volume of the target receiving the prescribed dose. Mean values with standard error of the parameters were computed for every group.

Statistical analysis was done with Statistica v.10 (StatSoft, Inc., Tulsa, USA). Differences with a p value < 0.05 were regarded as significant. The Kruskal-Wallis non-parametric test was used to compare values in groups.

In order to present the total progress made in APBI procedure, we proposed a plan quality index (PQI) defined as a sum of mean values of four evaluated parameters: PTV_{ref} normalized to 1, PTV_{min} normalized to 1, DHI, and COIN indexes. PQI was calculated for every group of patient.

Table 1. Implant characteristics, volume, and dose parameters

Parameter	Mean value	Range
Number of catheters	14	7-18
Number of planes	3	2-5
V_{PTV} [cm ³]	71.6	17.4-226.5
PTV_{ref} [%]	93.7	69.9-99.1
D_{90} [%]	106.0	66-122.9
PTV_{min} [%]	66.4	23.5-87.8
COIN	0.69	0.37-0.84
DHI	0.66	0.40-0.78
Skin D_{max} [%]	43.4	17.0-70.0
Ipsilateral lung D_{max} [%]	51.1	4.6-87.5
Ipsilateral lung D_2 [%]	41.2	13.0-68.3
Ipsilateral lung D_{10} [%]	31.7	10.0-55.0

Results

Implant characteristics, dose-volume parameters and critical organs doses are shown in Table 1. The mean volume of the PTV was 71.6 cm³. Generally, three-plane implants were made with the mean value of catheters equal 14. The mean values of target coverage with prescribed dose (PTV_{ref}) was 93.7%, minimum dose in the target volume (PTV_{min}) was 66.4%, and the dose encompassing 90% of the PTV (D_{90}) was 106%. The mean values of implant characterizing indices were acceptable, and they came to 0.69 for conformity index (COIN) and 0.66 for homogeneity index (DHI).

The mean value of maximum skin dose was 43.3% of the prescribed dose. The mean value of ipsilateral lung

Table 2. Mean values of parameters with standard deviations for groups presenting the consecutive periods of time

	Number of cases	PTV _{ref} [%]	PTV _{min} [%]	DHI	COIN	PQI
[I] 01-06.2009	8	83.4 ± 9.4	51.7 ± 13.7	0.53 ± 0.09	0.58 ± 0.13	2.46 ± 0.45
[II] 07-12.2009	15	91.1 ± 5.7	64.0 ± 13.0	0.59 ± 0.07	0.57 ± 0.08	2.71 ± 0.34
[III] 01-06.2010	21	93.3 ± 5.3	68.3 ± 14.9	0.67 ± 0.08	0.62 ± 0.10	2.90 ± 0.38
[IV] 07-12.2010	22	95.4 ± 1.7	70.1 ± 8.8	0.68 ± 0.05	0.60 ± 0.06	2.93 ± 0.22
[V] 01-06.2011	24	94.8 ± 3.7	68.9 ± 12.5	0.66 ± 0.08	0.71 ± 0.04	3.01 ± 0.28
[VI] 07-12.2011	37	93.9 ± 3.1	65.4 ± 8.6	0.67 ± 0.06	0.75 ± 0.04	3.01 ± 0.22
[VII] 01-06.2012	34	94.7 ± 2.9	67.3 ± 9.6	0.68 ± 0.06	0.76 ± 0.06	3.06 ± 0.25
[VIII] 07-12.2012	30	94.8 ± 1.7	66.0 ± 10.7	0.68 ± 0.07	0.74 ± 0.05	3.02 ± 0.24
<i>p</i> (Kruskal-Wallis)	–	0.0015	0.0115	0.0000	0.0000	–

dose to 2 cc volume was 41.2% of the prescribed dose, and the lung dose to a 10 cc volume was 31.7%; however, the maximum dose for ipsilateral lung was 51.1% on average. Recently, the maximum dose for the ribs surface is evaluated, though it is not taken into consideration in this study.

Table 2 and the Figures 1-4 show the evaluated parameters divided into groups presenting the consecutive periods of time. The data present mean value of analyzed parameters with standard deviations. The differences between groups are statistically significant, as *p* value is lower than 0.05 for every parameter evaluated.

PTV_{ref} have increased from mean value of 83.4% at the beginning to recent 94.8%. The maximum value equals 95.4% (Fig. 1). The same trend can be observed with PTV_{min} value, which has been improved from 51.7% to maximally 70.1% (Fig. 2). DHI and COIN mean values (Figs. 3 and 4) present the similar progress. DHI value increased from 0.53 level to 0.68, and COIN from 0.58 in 2009 to 0.74 lately.

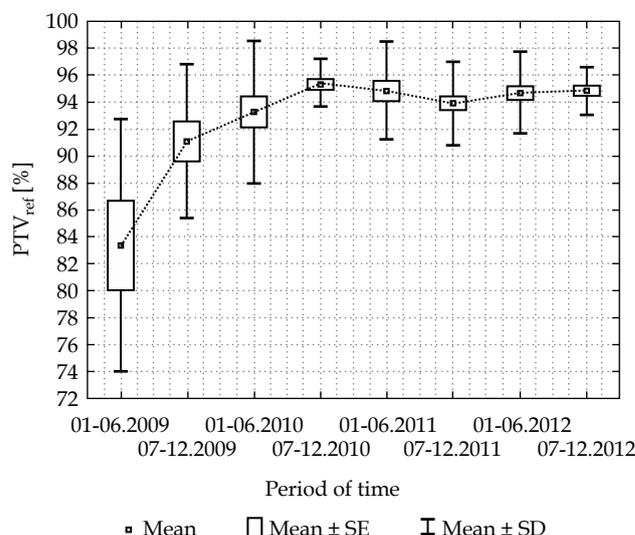


Fig. 1. Mean value of PTV_{ref} in the consecutive periods of time

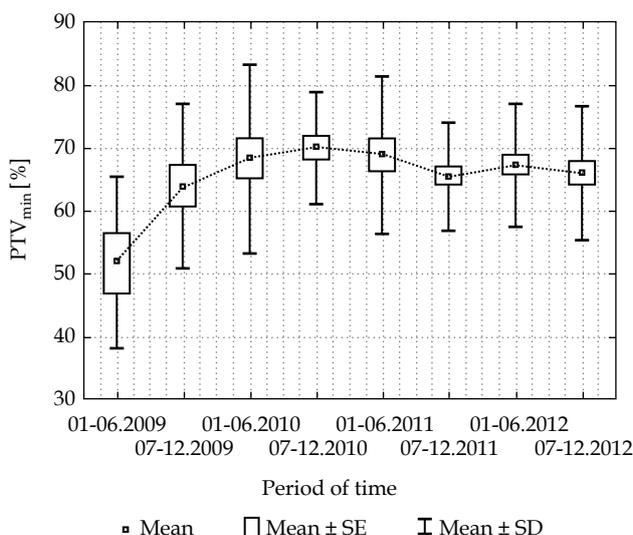


Fig. 2. Mean value of PTV_{min} in the consecutive periods of time

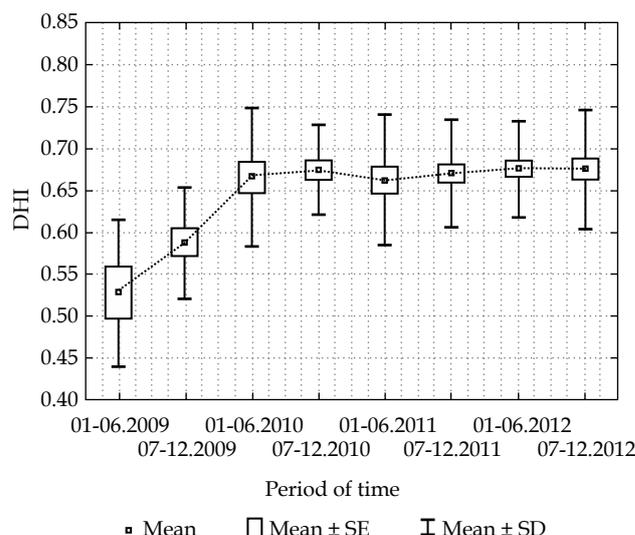


Fig. 3. Mean value of DHI in the consecutive periods of time

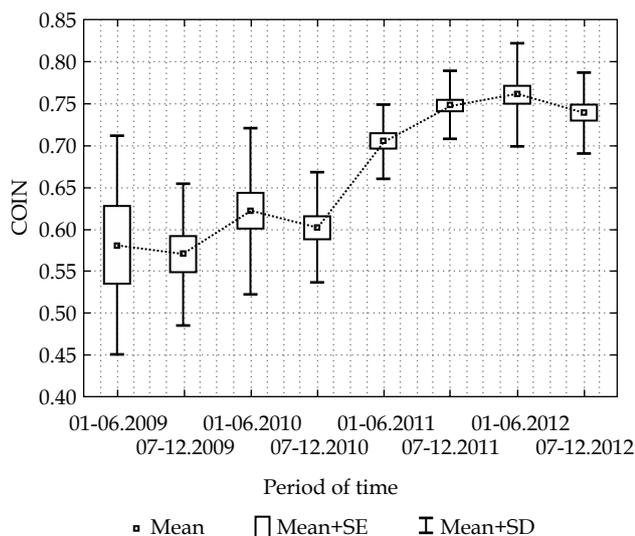


Fig. 4. Mean value of COIN in the consecutive periods of time

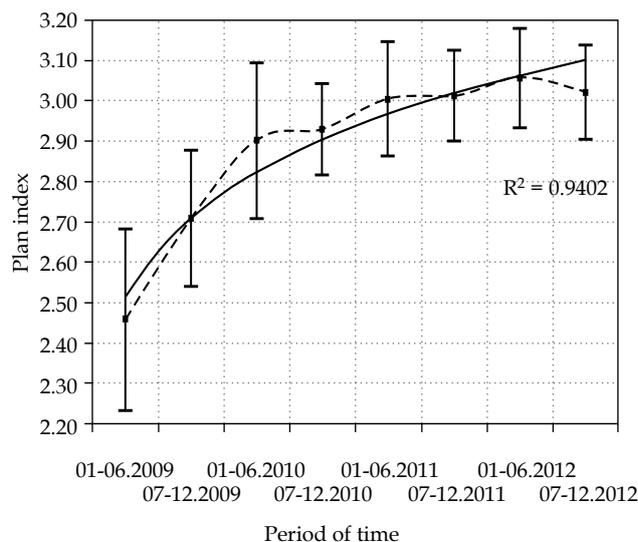


Fig. 5. Plan quality index value in the consecutive periods of time

Discussion

In multicatheter interstitial APBI, the precise target definition and implant quality are crucial for accurate and conformal delivery of the prescribed dose to the PTV, with simultaneous sparing of normal tissue and organs at risk [2,7,8,11,17,18]. Our results confirm these findings. From the very beginning, APBI technique in all over the world is being constantly improved in order to achieve good results with acceptable dosimetric parameters.

To improve dose distributions, dose optimization algorithms can be used. However, modification of the dwell times may produce overdose areas inside the treated volume [3,22,24]. Kestin *et al.* [20] have shown in their study that adding a few dwell positions improved target coverage from 87% to 97% of prescribed dose. Nevertheless, volume of tissue receiving 150% of the prescribed dose also increased.

From all factors that have influence the dose distribution, implant quality should be listed at the first place. We confirmed that improvement in implant quality increases the dose distribution conformity and homogeneity without extensive use of the optimization algorithms. That explains the requirement of use the accurate imaging method for treatment planning and pre-planning procedures. Two-dimensional orthogonal-based imaging has been replaced with CT-based three-dimensional [2,11,24]. CT-guided implantation improves dose distribution allowing the needles to be inserted precisely with respect to the target volume. Vicini *et al.* [19] demonstrated that CT-based dosimetry is needed to evaluate target coverage. Polgár and Major [26] emphasized that in modern brachytherapy, the treatment planning and plan evaluation have to be based on the 3D volume of the PTV, even though the use of a two-film localization technique allows the reconstruction of the catheters in three dimensions.

Many studies demonstrate beneficial effect of 3D imaging on dosimetric parameters of treatment plan, and discourage form using traditional two-dimensional implantation techniques for interstitial brachytherapy [19-21,

24,25]. The accuracy of dose delivery can be significantly improved with the use of 3D imaging before or during implantation. Vicini *et al.* [19] has conduct a study in which they selected patients who underwent CT scanning after implant placement to evaluate executed dose distribution with respect to delineated target volume. A median of only 68% of this volume received 100% of the prescribed dose. Major *et al.* [22,24,26] have compared dosimetric parameters achieved by replacing fluoroscopy-based needles implantation with CT-based one. All evaluated parameters have increased (70% vs. 91% for PTV_{100} , 0.35 vs. 0.33 for DNR, 0.40 vs. 0.68 for COIN) and improved the quality of the implants significantly. Cuttino *et al.* [25] reported that changing traditional two-dimensional techniques to a CT-guided technique caused mean target coverage (defined as the percentage of PTV with 2 cm margin receiving 90% of the prescribed dose) to increase from 42% to 93%, and mean DHI to increase from 0.77 to 0.82.

Since three-dimensional preplanning has been introduced in our institute with the additional acquisition after inserting one plane of the needles, target coverage has improved significantly [2]. With such procedures we are able to gain treatment plan dosimetric parameters comparable to other institutions achievements. Recently, it has been about 95% for PTV_{ref} , 66% for PTV_{min} , 0.68 for DHI, and 0.75 for COIN index.

In brachytherapy planning it is highly recommended to deliver at least the prescribed dose to the target with acceptable homogeneity and conformity of the dose distribution [2,23]. However, in some situations acceptable target coverage excludes satisfactory homogeneity and conformity of the dose distribution, so finding a balance between these parameters is required. Our results confirm these findings. It can be seen, for every parameter evaluated, that the mean value has reached the required level at one point, and then it has been oscillating around it. It means that the chosen parameter's value is higher in one period and lower in another one. However, higher value of one parameter usually effects lower value of another one during the treatment

planning. That prompted us to calculate the plan quality index as the sum of mean values of four evaluated parameters: PTV_{ref} normalized to 1, PTV_{min} normalized to 1, DHI, and COIN indexes. Figure 5 shows the plan quality index mean value in the consecutive periods of time.

From the beginning of three-dimensional era in our institute (two-dimensional era is not taken into account in this paper), the plan quality index has become higher. Plan quality index maximum value can be 4. However, it is not possible to achieve it in practice. In our institute plan quality index value has increased from 2.46 to 3.06, maximally. High correlation with the logarithmic trend curve with R^2 comes to 0.94 can be observed. That proves how hard we try to improve dose distributions.

Conclusions

According to ESTRO and ASTRO recommendations, reporting dosimetric parameters of implant as well as surrounding organs exposure to risk are obligatory. However, there are still no guidelines determining the required level of some parameters in brachytherapy of breast cancer. It is highly recommended to deliver at least the prescribed dose to the target with acceptable homogeneity and conformity of the dose distribution. The implant quality is crucial for the accurate dose distribution. This paper shows the progress we've made in APBI procedure to improve implant quality. It can be seen that nowadays our implant technique based on three-dimensional CT imaging results in acceptable dose distributions.

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