



CyberKnife versus multicatheter interstitial brachytherapy for accelerated partial breast irradiation: a dosimetrical assessment with focus on organs at risk

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ABSTRACT

Background: The purpose of the study was to dosimetrically compare multicatheter interstitial brachytherapy (MIBT) and stereotactic radiotherapy with CyberKnife (CK) for accelerated partial breast irradiation with special focus on dose to organs at risk (OARs).

Materials and methods: Treatment plans of thirty-one patients treated with MIBT were selected and additional CK plans were created on the same CT images. The OARs included ipsilateral non-target and contralateral breast, ipsilateral and contralateral lung, skin, ribs, and heart for left sided cases. The fractionation was identical (4×6.25 Gy). Dose-volume parameters were calculated for both techniques and compared.

Results: The D90 of the PTV for MIBT and CK were similar (102.4% vs. 103.6%, $p = 0.0654$), but in COIN the MIBT achieved lower value (0.75 vs. 0.91, $p < 0.001$). Regarding the V100 parameter of non-target breast CK performed slightly better than MIBT (V100: 1.1% vs. 1.6%), but for V90, V50 and V25 MIBT resulted in less dose. Every examined parameter of ipsilateral lung, skin, ribs and contralateral lung was significantly smaller for MIBT than for CK. Protection of the heart was slightly better with MIBT, but only the difference of $D2cm^3$ was statistically significant (17.3% vs. 20.4%, $p = 0.0311$). There were no significant differences among the dose-volume parameters of the contralateral breast.

Conclusion: The target volume can be properly irradiated by both techniques with high conformity and similar dose to the OARs. MIBT provides more advantageous plans than CK, except for dose conformity and the dosimetry of the heart and contralateral breast. More studies are needed to analyze whether these dosimetrical findings have clinical significance.

Key words: multicatheter interstitial brachytherapy; CyberKnife; APBI; dosimetrical comparison

Rep Pract Oncol Radiother 2022;27(1):152-160

Introduction

Over the last decades, breast conserving surgery followed by postoperative radiotherapy has

obtained broad acceptance among radiation oncologists for treating early stage breast cancer [1]. Nowadays, for a selected group of patients, accelerated partial breast irradiation (APBI) is an available

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technique instead of conventional whole breast irradiation (WBI) [2]. For APBI the irradiated volume is smaller compared to WBI, so patients can tolerate a higher fraction dose; consequently, the total treatment time for APBI is 4–5 days (instead of 3–5 weeks of conventional WBI) and, therefore, it is a very attractive option among patients. Furthermore, because of the smaller irradiated volume the doses to normal tissues are decreased compared to the WBI.

Different techniques are available for APBI with the same aim to create conformal, homogenous dose distributions and to offer short overall treatment time [3]. The first technique was the multicatheter interstitial brachytherapy (MIBT) which has excellent clinical results with the longest follow up [4–11]. For MIBT, there are recommendations for patient selection [12] and target volume definition [13, 14]. For the proper quality assurance of this technique, there are also practical guidelines available [15, 16]. For APBI among brachytherapy (BT) techniques, other modalities are also available, such as single or multichannel balloon therapy and seed implantation. Regarding the external beam radiotherapy (EBRT) for APBI, 3D conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), volume modulated arc therapy (VMAT), helical tomotherapy, CyberKnife therapy (CK), proton therapy and, as intraoperative methods, irradiation by electrons or low energy photons are to be mentioned [17, 18]. Since these techniques are routinely used in clinics, all of them provide appropriate dose coverage and normal tissue sparing, but they slightly differ in dose distribution, invasiveness and treatment delivery.

For APBI with CK, several dosimetrical comparisons were performed. There are studies comparing CK with 3D-CRT [19–24], with IMRT [19,23,24], with VMAT [22, 23] and even with tomotherapy [21]. There are papers about comparison of MIBT against 3D-CRT [25], IMRT [26] and VMAT [27]. Our group published two papers about dosimetry of CK against MIBT, one comparing clinical CK plans with hypothetical MIBT plans [28] and another one with comparison between clinical plans from both techniques [29].

The goal of this study was to complete our investigations in this topic by performing the third type of dosimetrical comparison between the MIBT and CK for APBI using clinical MIBT plans and hypo-

thetic CK plans with identical CT images and critical structures with special focus on dose to organs at risk (OAR-s).

Materials and methods

Multicatheter interstitial brachytherapy

Treatment plans of thirty-one patients treated with MIBT at our institute were selected for dosimetrical comparison. Thirteen patients (42%) had right sided and eighteen (58%) left sided tumour. Among the thirty-one patients, eighteen (58%) had tumours in the upper quadrant of which twelve (39%) were in the inner and six (19%) in the outer quadrant. Out of the thirteen (42%) lower quadrant tumours, nine (29%) were in the inner and four (13%) in the outer quadrant. The treatment plans were optimised with an inverse optimisation method (Hybrid Planning Optimization — HIPO), and these plans were used for the treatments and for the comparison. The treatments were performed by a high-dose-rate afterloader (microSelectron V3, Elekta, Brachytherapy, Veenendaal, The Netherlands) with Ir-192 stepping source. The GEC-ESTRO guidelines were followed for patient selection and target volume definitions [12, 14]. For treatment planning Oncentra Brachy v4.3 planning system (Elekta, Brachytherapy, Veenendaal, The Netherlands) was used with calculation algorithm of the TG-43 formalism [30]. The mean catheter number was 15 (range, 7–28).

CT scans with 3 mm slice distance were acquired for target definition and treatment planning. During lumpectomy surgical clips were placed in the cavity wall which help the delineation of lumpectomy cavity. 20 mm safety margin (surgical plus irradiation) was added to the lumpectomy cavity to get the CTV in all main six directions [14]. The CTV was always limited in the breast, no skin, thoracic wall, and pectoral muscles were included. The PTV was always equal to CTV. The outlined and examined OARs were as follows: the ipsilateral and contralateral lungs and breasts, heart (in the left sided cases), skin and ribs. An additional volume, the non-target breast was created from the ipsilateral breast with a subtraction of the PTV. The skin was defined as a 5 mm layer below body surface.

The required target coverage was at least 90% by the prescribed dose (PD) while keeping the

dose distribution as homogenous as possible. To quantify the dose homogeneity, the dose-nonuniformity ratio (DNR) was used, which is the ratio of volumes irradiated by 1.5 times of the PD and the PD ($V_{1.5 \times PD}/V_{PD}$). The constraint for DNR was less than or equal to 0.35. The target coverage was prioritized if the dose coverage and the homogeneity constraints could not be fulfilled at the same time. Dose objective was applied for the skin during treatment planning, the surface skin dose was maximized in 70% of the PD to avoid skin toxicity. For the other OARs the parameters were only registered. The PD was 25 Gy (4×6.25 Gy) and the irradiation time ranged between 5-15 min depending on the activity of the source.

CyberKnife treatments

For CK planning, the same CT data sets with the same contours as for MIBT were used except for the PTV. To imitate the real CK treatments, a 2 mm additional margin to CTV was used to create PTV according to our clinical protocol [31]. For evaluation purpose, PTV_EVAL was created from PTV with subtraction of the skin layer if needed. The prescribed dose was the same as in MIBT. The CT slice thickness was resampled to 1.25 mm because this resolution is routinely used in our clinic for CK planning in the Precision 2.0.0.1 (Accuray, Sunnyvale, CA, USA) software. VOLO optimization method using InCise 2TM MLC method with step-and-shoot IMRT technique was applied with a finite size pencil beam (FSPB) dose calculation algorithm for optimization and plan evaluation. During the optimization, the contralateral breast and lung were allowed with “exit only” direction to avoid the beams with very long path in the body from the surface to the PTV. The aim was to achieve at least 99.5% of V95 for PTV_EVAL and keep the maximum point dose under 115% of the PD [31]. Our acceptance criteria for OARs were as follows: $V50 \leq 50$ for NTB, $D2cm^3 \leq 70$ for ipsilateral lung, $D2cm^3 \leq 45$ for heart, $D1cm^3 \leq 100$ for both skin and ribs, and $D0.1cm^3 \leq 10$ for contralateral breast. Three shells (one voxel thick ring ROI 4 mm, 15 mm and 25 mm away from the PTV) were used to ensure the high conformity and high dose gradient of the dose distribution. All of the treatment plans were clinically acceptable according to our institutional protocol [31].

The calculated mean estimated treatment time was 31.1 min (range, 26–37 min).

Dosimetrical evaluation and statistical analysis

The dose volume histograms (DVHs) were the basis of the treatment plan evaluation. The relative (eg. V100) and absolute volumes [eg. V100 (cm³)] receiving a percentage of the PD (eg. 100%) were calculated. Furthermore, the relative doses of the PD in percentage to relative volumes (eg. D5 for 5%) and to absolute volumes (eg. D1cm³) were calculated. The conformity of dose distribution was characterized with the COIN [32].

For reporting of the treatment plans, descriptive statistics were calculated. Shapiro-Wilk-W-test was used on dose-volume parameters' distributions to test normality. The Wilcoxon-Matched-Pairs-Test was used for comparisons with Statistica 10.0 software (StatSoft, Inc., Tulsa, OK, USA), because almost none of the parameters followed the normal distribution. The $p < 0.05$ value was stated statistically significant. All the patients were treated according to our institutional protocol, and in this dosimetrical study we retrospectively collected and evaluated the treatment planning data, so no ethical approval was needed.

Results

The mean volume of the ipsilateral breast was 817.1 cm³ (range, 386.9–2097.5 cm³). The mean volume of the PTV was 59.1 cm³ (range, 26.6–173.6 cm³) for MIBT plans and 82.3 cm³ (range, 40.3–223.3cm³) for CK plans which was significantly higher ($p < 0.0001$). For MIBT the V100 for PTV was 91.6% (range, 87.9–96.4%) meanwhile the DNR was 0.35 (range, 0.24–0.44). For PTV_EVAL of CK patients the V100 and V95 was 98.9% (range, 96.4–99.9%) and 99.9% (range, 99.9–100%), respectively, and the mean of the maximum dose was 114.5% (range, 111.1–117.6%). The D90 value was 102.4% (range, 95.9–112.1%) for MIBT and 103.6% (range, 102.3–105.2%) for CK without statistical significance ($p = 0.0654$).

The absolute volumes encompassed by the reference dose (100%), 0.5 times and 0.2 times the reference dose (V_{ref} , $V_{0.5ref}$, $V_{0.2ref}$) were significantly smaller for MIBT than for CK as shown in Table 1. But related these volumes to the volume of the PTV the ratios of V_{ref}/V_{PTV} , $V_{0.5ref}/V_{PTV}$ and $V_{0.2ref}/V_{PTV}$ are

Table 1. Dosimetry of organs at risk for multicatheter interstitial brachytherapy (MIBT) and CyberKnife (CK) treatments. Significant p-values are in bold

Structure	Parameter	MIBT	CK	p-value*
Body	V _{ref} (cm ³)	67.1 (28.9–193.8)	88.5 (45.6–238.0)	< 0.0001
	V _{0.5ref} (cm ³)	160.5 (73.4–444.2)	236.4 (138.1–531.1)	< 0.0001
	V _{0.2ref} (cm ³)	473.0 (253.4–1078.1)	657.7 (395.1–1205.0)	< 0.0001
PTV	V100 (%)	91.6 (87.9–96.4)	98.9 (96.4–99.9)	< 0.0001
	V90 (%)	96.2 (93.5–98.5)	99.9 (99.9–100.0)	< 0.0001
	D98 (%)	84.2 (74.8–108.5)	100.9 (98.8–102.6)	< 0.0001
	D90 (%)	102.4 (95.9–112.1)	103.6 (102.3–105.2)	0.0654
	D50 (%)	138.7 (126.2–182.2)	107.7 (106.3–109.6)	< 0.0001
	D2 (%)	472.0 (402.2–548.4)	112.2 (109.6–114)	< 0.0001
Non-target breast	V100 (%)	1.6 (0.4–4.2)	1.1 (0.2–4.3)	0.0002
	V90 (%)	2.7 (0.6–8.1)	4.6 (0.9–13.2)	< 0.0001
	V50 (%)	12.6 (3.1–35.4)	18.0 (4.8–43.1)	< 0.0001
	V25 (%)	31.4 (9.4–68.4)	37.5 (12.2–59.5)	0.0011
Ipsilateral lung	MLD (%)	4.9 (1.9–11.1)	6.2 (1.3–12.2)	< 0.0001
	D0.1cm ³ (%)	41.2 (10.1–61.5)	56.2 (9.0–78.8)	< 0.0001
	D1cm ³ (%)	36.2 (8.7–55.8)	49.8 (8.1–70.6)	< 0.0001
	D2cm ³ (%)	33.8 (8.0–52.5)	46.7 (7.6–67.2)	< 0.0001
	V5 (%)	30.6 (5.1–50.0)	38.0 (2.2–77.6)	0.0001
Skin	D0.1cm ³ (%)	70.9 (21.8–164.2)	82.3 (38.2–105.6)	0.0005
	D0.2cm ³ (%)	66.6 (21.0–140.7)	80.1 (36.4–104)	0.0004
	D1cm ³ (%)	55.9 (18.1–97.1)	72.1 (29.6–98.9)	< 0.0001
Ribs	D0.1cm ³ (%)	54.1 (8.1–92.7)	71.2 (7.6–100.2)	< 0.0001
	D1cm ³ (%)	43.3 (5.3–76.4)	60.3 (5.8–93.4)	< 0.0001
	V50 (cm ³)	2 (0.0–16.4)	3.4 (0.0–10.3)	0.0018
Heart	MHD (%)	4.1 (1.0–7.7)	5.4 (0.3–12.9)	0.0641
	D0.1cm ³ (%)	21.8 (4.0–47.2)	23.4 (2.3–49.6)	0.1988
	D1cm ³ (%)	18.6 (3.2–42.3)	21.3 (2.0–44.8)	0.0526
	D2cm ³ (%)	17.3 (3.0–40.0)	20.4 (1.8–43.9)	0.0311
	V5 (%)	29.9 (0.0–62.5)	40.2 (0.0–93.6)	0.0641
Contralateral breast	D0.1cm ³ (%)	4.2 (0.0–9.8)	3.4 (0.1–8.7)	0.4927
	D1cm ³ (%)	2.7 (0.0–6.4)	3.1 (0.1–7.8)	0.1950
Contralateral lung	D0.1cm ³ (%)	5.7 (1.7–11.7)	6.9 (1.6–11.8)	0.0186
	D1cm ³ (%)	3.8 (0.0–8.3)	6.1 (1.1–10.4)	0.0001

*Wilcoxon matched pair test

1.16 vs. 1.08 (p = 0.001), 3.17 vs. 3.39 (p = 0.002) and 9.33 vs 9.44 (p = 0.5306) for MIBT and CK, respectively.

The dose conformity was very high for both techniques (Fig. 1). The V100 value of non-target breast was greater for MIBT than for CK: 1.6% (range, 0.4–4.2%) vs. 1.1% (range, 0.2–4.3%), p = 0.0002, but the other dosimetrical parameters for ipsilateral non-target breast were smaller for MIBT. The high

dose conformity for both techniques is demonstrated by large conformity indices. The COIN was 0.75 for MIBT and 0.91 for CK patients (p < 0.001).

All examined parameters of the ipsilateral lung, skin and ribs were significantly smaller for MIBT. The maximal dose to the ribs never exceeded the PD in MIBT plans [V100(cm³) = 0], and among CK plans there was only 1 case when the 100% isodose line reached the rib.

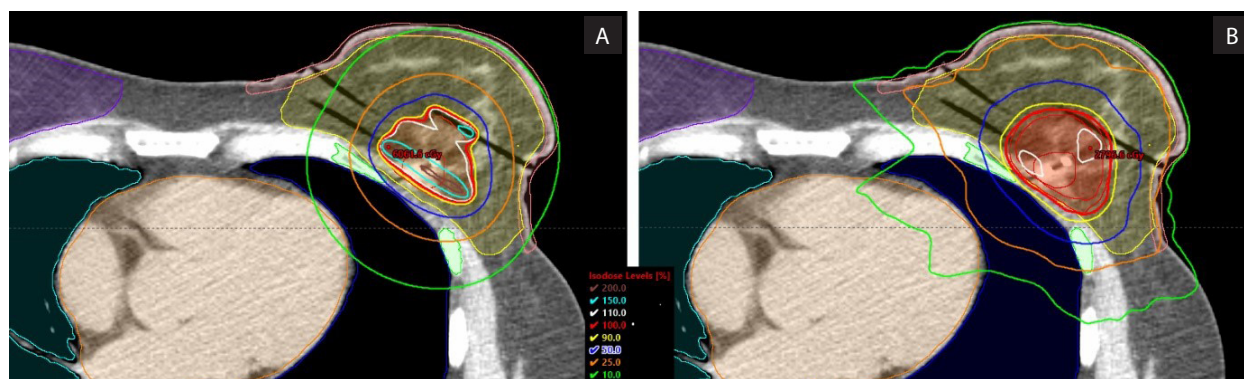


Figure 1. Representative comparative dose distributions for multicatheter interstitial brachytherapy (MIBT) (A) and CyberKnife (CK) treatment (B). Planning target volume (PTV): red, ipsilateral breast: yellow, contralateral breast: pink, ribs: green, heart: orange, ipsilateral lung: dark blue, contralateral lung: light blue, skin: tomato

In heart dosimetry of patients with left-sided lesions, MIBT provided less doses, but the difference was significant only for $D2\text{cm}^3$ (17.3% vs. 20.4%, $p = 0.0311$) in favour of MIBT.

For contralateral breast and lung, volumetric dose parameters were very low for both techniques, but MIBT resulted in significantly lower values in the case of contralateral lung, but for contralateral breast the difference was not significant. The detailed dosimetrical results can be found in Table 1.

Discussion

During the last decades several techniques have been introduced for APBI, and obviously the question is interesting which option is the best for patients. The last one in the line of the techniques is the CK, the first report on using stereotactic radiotherapy for breast tumours was published by Bondiau et al. in 2009 [33]. The feasibility of APBI treatments with CK was confirmed by studies, Vermeulen et al. reported about nine APBI patients treated with CK in 2011 and about 21 patients in 2014 [34, 35]. In another retrospective study the dosimetrical results of 10 CK treated patients were analyzed by Obayomi et al. [36]. Lozza et al. [37] reported mainly the clinical results of a study with twenty APBI patients treated with CK. Several papers have been published about comparisons between different APBI techniques, CK comparing other external beam techniques [19–24], and MIBT against external beam techniques [25–27]. There is no consensus on which comparison method should be used for making judgement on different irradiation techniques. There are studies in which either

BT [26] or EBRT [27, 28] CT images are used as a reference image set for comparison. Another way of comparison is when separate patient cohorts of two different techniques are analyzed [29,38]. Our group has published two papers about MIBT against CK, Fröhlich et al. [28] performed a matched pair analysis of treatment plans using CT scans taken for CK and Herein et al. [29] compared clinical plans of separate patient groups of both techniques. In this paper we completed our previous investigation of APBI with a matched pair analysis of treatment plans of CK and MIBT, using the MIBT datasets.

APBI treatment with CK is feasible and produce usually better dosimetrical parameters of the OARs compared to other external beam techniques [19–21]. In a very thorough analysis of nine patients examining 3D-CRT against CK with Iris and Multileaf collimator Goggin et al. [20] found that CK gives better parameters for the lung and ipsilateral breast, except for the V5 of lung. The V5 for the lung was significantly lower for 3D-CRT than for CK-Iris and CK-Multileaf, 6.2% vs. 39.4% and 17.9%, respectively. Xu et al. [19] examined CK against 3D-CRT and IMRT and found CK to be more conformal than the other two techniques. They reported better dose sparing for OARs of CK except for the extremely low dose region. Furthermore, the ratio of V20% to V100% of the breast was the smallest for CK. Rault et al. [21] examined the effect of respiratory tracking on dosimetry of OARs. They compared CK against Tomotherapy and 3D-CRT, and found dosimetrical advantages in dose to non-target breast for the CK which was the consequence of the non-coplanar beams. In a ten patient study, Bonfantini et al. [22] compared CK

against 3D-CRT and VMAT. Except for the heart, they found significant differences in OARs dosimetry. Based on their analysis 3D-CRT gives reduction of the dose to OAR-s except for ipsilateral breast where V50 was significantly lower for CK than for 3D-CRT (16.3% vs. 26.0%, $p < 0.01$).

Major et al. [26] compared MIBT against coplanar IMRT showing that MIBT provides better normal tissue sparing (except for the heart) than IMRT. Similar to our current work they created IMRT plans on MIBT CT-datasets and contours and performed a matched pair analysis for comparison. Weed et al. [38] examined MIBT against MammoSiteTM and 3D-CRT techniques and found that doses to the breast tissue were significantly lower for both BT techniques (except for the volume irradiated by the PD) compared to 3D-CRT.

CyberKnife can provide dose distributions with steep dose fall-off around PTV because of the non-coplanarity of many used treatment fields, likewise in MIBT where the similar dose distributions outside the PTV occur because of the high dose gradient around BT sources. Inside the PTV, there are large differences, the maximum dose in CK is aimed to be under 115% of PD but the most exposed small volumes in MIBT can be over 400% of PD. In our examination the similar D90 value for PTV (102.4% vs. 103.6% for MIBT and CK, respectively, $p = 0.0654$) served as a base for the comparison of treatment plans of the two techniques, so we focused to the OAR's dosimetry. The absolute volumes in whole body irradiated by the PD (V_{ref}), 50% of PD ($V_{0.5ref}$) and 20% of PD ($V_{0.2ref}$) are significantly larger for CK as shown in Table 1, which is the consequence of the significantly bigger volume of the PTV of CK (59.1 cm³ vs. 82.3 cm³ for MIBT and CK, respectively, $p < 0.0001$). But the ratio of the irradiated volume by PD, 50% of PD and 20% of PD to the PTV, which clearly refers to the technique, reveals that for high doses CK provides better values (V_{ref}/V_{PTV} for MIBT and CK are 1.16 and 1.08, $p = 0.001$). For smaller doses (50% of PD and 20% of PD) MIBT irradiates smaller volumes even relative to the PTV, but the difference is significant only in the case of 50% of PD. Based on these observations, the similarity of the dose distribution outside the PTV (except for high doses) can be considered to be confirmed. For non-target breast we found CK better only in the V100 parameter (1.6% vs. 1.1% for MIBT and CK, respectively, $p = 0.002$),

which means a better conformity of CK plans, but we received significantly higher values at smaller doses (V90, V50 and V25) for CK compared to MIBT. This is similar to what Fr hlich et al. [28] found in a matched pair analysis where the V50 value was 3.3% vs. 10.5% for MIBT and CK, respectively. The very small value of V50 for MIBT can be attributed to the ideal implant of virtual MIBT plans. Furthermore, Herein et al. [29] found that with comparison of clinical plans every examined parameter of non-target breast is lower for CK. That is because in that comparison the mean volume of PTV of CK plans was 71.7 cm³, while in this study this value was 82.3 cm³. We found every examined parameter of the ipsilateral lung significantly lower for MIBT than for CK, and this was true for the most exposed small volumes (D0.1cm³, D1cm³) in other two comparisons as well [28, 29]. For the skin and ribs, we also found significantly lower doses in every examined parameter for MIBT than for CK. In heart dosimetry we obtained smaller values in every examined parameter for MIBT than for CK, but only the D2cm³ was significantly different. By the comparison of clinical plans, CK produced smaller volumes in every examined parameter of the heart without statistical significance [29], and in the other matched pair analysis CK provided smaller doses in the examined two parameters (D0.1cm³ and D1cm³), but only the D0.1cm³ was significantly different. The strongest effect of the lesion's position can be expected in the case of heart dosimetry, so the matched pair analysis, which is based on the same anatomy, is more valid to discover the differences between parameters of the two techniques. But based on the matched pair analysis there is no clear result. Current study found slightly smaller values for MIBT than for CK, while Fr hlich et al. [28] found significantly smaller D0.1cm³ parameter for CK (12.8% vs. 12.1% for MIBT and for CK, respectively, $p = 0.0476$). For the contralateral breast and lung, very low values were found. Current study found only significant differences in parameters of the contralateral lung, MIBT produced smaller D.01cm³ and D1cm³ values than CK (5.7% vs. 6.9% ($p = 0.0186$) and 3.8% vs. 6.1% ($p = 0.0001$), respectively). For the contralateral breast, no significant differences were obtained.

The limitation of our study is that the dosimetric evaluation was performed by the comparison of real clinical and theoretical treatment plans. But

the existing differences between the two techniques could be discovered mainly with this method, because in this way there are no differences in patient characteristics and individual anatomy, and the differences reflect the dosimetrical characteristics of the two techniques only. The CK plans were not made on the same anatomy as would be the case in a real clinical situation due to the slightly pressed breast by the fixation buttons of implanted catheters. Consequently, the shape of the breast and the body contour is different from the real condition of CK treatment, which is a consequence of this type of comparing technique. It has to be also mentioned that the catheters and markers used in the MIBT technique induce a small tissue inhomogeneity effect, but the changes in dosimetry are around 0.5%, so there is no relevant influence of the catheters on the result [26].

Based on our findings MIBT protects better the OARs than CK, except for the contralateral breast, where significant differences could not be established; however, the dosimetrical parameters of CK plans are also clinically acceptable. In the light of the superior dosimetric parameters of MIBT and based on the long-term clinical evidence [6], MIBT should still be the first choice of APBI regarding the dose to OARs in well selected patients.

Conclusions

In APBI the dose distributions of MIBT and CK are similar regarding doses smaller than the PD; both techniques provide appropriate dose coverage of the PTV, and there are small, but significant differences in some dosimetrical parameters of OARs. Based on our examinations, we conclude that all of the OARs can be better protected with MIBT, except for the contralateral breast and the non-target breast regarding the PD. Further clinical investigation would be needed to decide whether these small, but significant dosimetrical differences in OAR parameters have effect on clinical results.

Conflicts of interest

The authors report no conflict of interest.

Funding

This work was supported by the National Laboratories Excellence program (under the National Tumorbiology Laboratory project) and the Hungar-

ian Thematic Excellence Program (under projects TUDFO/51757/2019-ITM and TKP2020-NKA-26).

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Authors' contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by A.H., G.S. and T.M.. The first draft of the manuscript was written by A.H. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. Early Breast Cancer Trialists' Collaborative Group. Effects of Radiotherapy and Surgery in Early Breast Cancer — An Overview of the Randomized Trials. *N Engl J Med.* 1995; 333(22): 1444–1456, doi: [10.1056/nejm199511303332202](https://doi.org/10.1056/nejm199511303332202), indexed in Pubmed: [7477144](https://pubmed.ncbi.nlm.nih.gov/7477144/).
2. Polgár C, Major T. Current status and perspectives of brachytherapy for breast cancer. *Int J Clin Oncol.* 2009; 14(1): 7–24, doi: [10.1007/s10147-008-0867-y](https://doi.org/10.1007/s10147-008-0867-y), indexed in Pubmed: [19225919](https://pubmed.ncbi.nlm.nih.gov/19225919/).
3. Forster T, Köhler CV, Debus J, et al. Accelerated Partial Breast Irradiation: A New Standard of Care? *Breast Care (Basel).* 2020; 15(2): 136–147, doi: [10.1159/000506254](https://doi.org/10.1159/000506254), indexed in Pubmed: [32398982](https://pubmed.ncbi.nlm.nih.gov/32398982/).
4. Polgár C, Major T, Fodor J, et al. Accelerated partial-breast irradiation using high-dose-rate interstitial brachytherapy: 12-year update of a prospective clinical study. *Radiother Oncol.* 2010; 94(3): 274–279, doi: [10.1016/j.radonc.2010.01.019](https://doi.org/10.1016/j.radonc.2010.01.019), indexed in Pubmed: [20181401](https://pubmed.ncbi.nlm.nih.gov/20181401/).
5. Polgár C, Fodor J, Major T, et al. Breast-conserving therapy with partial or whole breast irradiation: ten-year results of the Budapest randomized trial. *Radiother Oncol.* 2013; 108(2): 197–202, doi: [10.1016/j.radonc.2013.05.008](https://doi.org/10.1016/j.radonc.2013.05.008), indexed in Pubmed: [23742961](https://pubmed.ncbi.nlm.nih.gov/23742961/).
6. Polgár C, Ott O, Hildebrandt G, et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive

- and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. *Lancet Oncol.* 2017; 18(2): 259–268, doi: [10.1016/s1470-2045\(17\)30011-6](https://doi.org/10.1016/s1470-2045(17)30011-6), indexed in Pubmed: [28094198](https://pubmed.ncbi.nlm.nih.gov/28094198/).
7. Strnad V, Ott O, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet.* 2016; 387(10015): 229–238, doi: [10.1016/s0140-6736\(15\)00471-7](https://doi.org/10.1016/s0140-6736(15)00471-7), indexed in Pubmed: [26494415](https://pubmed.ncbi.nlm.nih.gov/26494415/).
 8. Ott OJ, Strnad V, Hildebrandt G, et al. Groupe Européen de Curiethérapie of European Society for Radiotherapy and Oncology (GEC-ESTRO). GEC-ESTRO multicenter phase 3-trial: Accelerated partial breast irradiation with interstitial multicatheter brachytherapy versus external beam whole breast irradiation: Early toxicity and patient compliance. *Radiother Oncol.* 2016; 120(1): 119–123, doi: [10.1016/j.radonc.2016.06.019](https://doi.org/10.1016/j.radonc.2016.06.019), indexed in Pubmed: [27422584](https://pubmed.ncbi.nlm.nih.gov/27422584/).
 9. Soror T, Kovács G, Seibold N, et al. Cosmetic changes following surgery and accelerated partial breast irradiation using HDR interstitial brachytherapy: Evaluation by a multidisciplinary/multigender committee. *Strahlenther Onkol.* 2017; 193(5): 367–374, doi: [10.1007/s00066-016-1093-6](https://doi.org/10.1007/s00066-016-1093-6), indexed in Pubmed: [28044202](https://pubmed.ncbi.nlm.nih.gov/28044202/).
 10. Schäfer R, Strnad V, Polgár C, et al. Quality-of-life results for accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation in early breast cancer after breast-conserving surgery (GEC-ESTRO): 5-year results of a randomised, phase 3 trial. *Lancet Oncol.* 2018; 19(6): 834–844, doi: [10.1016/s1470-2045\(18\)30195-5](https://doi.org/10.1016/s1470-2045(18)30195-5), indexed in Pubmed: [29695348](https://pubmed.ncbi.nlm.nih.gov/29695348/).
 11. Vicini F, Cecchini R, White J, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *The Lancet.* 2019; 394(10215): 2155–2164, doi: [10.1016/s0140-6736\(19\)32514-0](https://doi.org/10.1016/s0140-6736(19)32514-0), indexed in Pubmed: [31813636](https://pubmed.ncbi.nlm.nih.gov/31813636/).
 12. Polgár C, Van Limbergen E, Pötter R, et al. GEC-ESTRO breast cancer working group. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). *Radiother Oncol.* 2010; 94(3): 264–273, doi: [10.1016/j.radonc.2010.01.014](https://doi.org/10.1016/j.radonc.2010.01.014), indexed in Pubmed: [20181402](https://pubmed.ncbi.nlm.nih.gov/20181402/).
 13. Strnad V, Hannoun-Levi JM, Guinot JL, et al. Working Group Breast Cancer of GEC-ESTRO. Recommendations from GEC ESTRO Breast Cancer Working Group (I): Target definition and target delineation for accelerated or boost Partial Breast Irradiation using multicatheter interstitial brachytherapy after breast conserving closed cavity surgery. *Radiother Oncol.* 2015; 115(3): 342–348, doi: [10.1016/j.radonc.2015.06.010](https://doi.org/10.1016/j.radonc.2015.06.010), indexed in Pubmed: [26104975](https://pubmed.ncbi.nlm.nih.gov/26104975/).
 14. Major T, Gutiérrez C, Guix B, et al. Breast Cancer Working Group of GEC-ESTRO. Recommendations from GEC ESTRO Breast Cancer Working Group (II): Target definition and target delineation for accelerated or boost partial breast irradiation using multicatheter interstitial brachytherapy after breast conserving open cavity surgery. *Radiother Oncol.* 2016; 118(1): 199–204, doi: [10.1016/j.radonc.2015.12.006](https://doi.org/10.1016/j.radonc.2015.12.006), indexed in Pubmed: [26776444](https://pubmed.ncbi.nlm.nih.gov/26776444/).
 15. Strnad V, Major T, Polgar C, et al. ESTRO-ACROP guideline: Interstitial multi-catheter breast brachytherapy as Accelerated Partial Breast Irradiation alone or as boost - GEC-ESTRO Breast Cancer Working Group practical recommendations. *Radiother Oncol.* 2018; 128(3): 411–420, doi: [10.1016/j.radonc.2018.04.009](https://doi.org/10.1016/j.radonc.2018.04.009), indexed in Pubmed: [29691075](https://pubmed.ncbi.nlm.nih.gov/29691075/).
 16. Strnad V, Krug D, Sedlmayer F, et al. Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guideline for partial-breast irradiation. *Strahlenther Onkol.* 2020; 196(9): 749–763, doi: [10.1007/s00066-020-01613-z](https://doi.org/10.1007/s00066-020-01613-z), indexed in Pubmed: [32350554](https://pubmed.ncbi.nlm.nih.gov/32350554/).
 17. Njeh CF, Saunders MW, Langton CM. Accelerated Partial Breast Irradiation (APBI): A review of available techniques. *Radiat Oncol.* 2010; 5: 90, doi: [10.1186/1748-717X-5-90](https://doi.org/10.1186/1748-717X-5-90), indexed in Pubmed: [20920346](https://pubmed.ncbi.nlm.nih.gov/20920346/).
 18. Stelczar G, Major T, Mészáros N, et al. External beam accelerated partial breast irradiation: dosimetric assessment of conformal and three different intensity modulated techniques. *Radiol Oncol.* 2019; 53(1): 123–130, doi: [10.2478/raon-2019-0001](https://doi.org/10.2478/raon-2019-0001), indexed in Pubmed: [30661060](https://pubmed.ncbi.nlm.nih.gov/30661060/).
 19. Xu Q, Chen Y, Grimm J, et al. Dosimetric investigation of accelerated partial breast irradiation (APBI) using CyberKnife. *Med Phys.* 2012; 39(11): 6621–6628, doi: [10.1118/1.4757616](https://doi.org/10.1118/1.4757616), indexed in Pubmed: [23127056](https://pubmed.ncbi.nlm.nih.gov/23127056/).
 20. Goggin LM, Descovich M, McGuinness C, et al. Dosimetric Comparison Between 3-Dimensional Conformal and Robotic SBRT Treatment Plans for Accelerated Partial Breast Radiotherapy. *Technol Cancer Res Treat.* 2016; 15(3): 437–445, doi: [10.1177/1533034615601280](https://doi.org/10.1177/1533034615601280), indexed in Pubmed: [26335703](https://pubmed.ncbi.nlm.nih.gov/26335703/).
 21. Rault E, Lacornerie T, Dang HP, et al. Accelerated partial breast irradiation using robotic radiotherapy: a dosimetric comparison with tomotherapy and three-dimensional conformal radiotherapy. *Radiat Oncol.* 2016; 11: 29, doi: [10.1186/s13014-016-0607-9](https://doi.org/10.1186/s13014-016-0607-9), indexed in Pubmed: [26919837](https://pubmed.ncbi.nlm.nih.gov/26919837/).
 22. Bonfantini F, De Martin E, Giandini T et al. A Dosimetric Comparison between Three Different External Photon Beam Techniques for Accelerated Partial Breast Irradiation. *Clin Oncol* 2018;3:1501. <http://www.clinicsinoncology.com/full-text/cio-v3-id1501.php>.
 23. Lee C, Kim W, Kim H, et al. Dosimetric Plan Comparison of Accelerated Partial Breast Irradiation (APBI) Using CyberKnife. *Prog Med Phys.* 2018; 29(2): 73, doi: [10.14316/pmp.2018.29.2.73](https://doi.org/10.14316/pmp.2018.29.2.73).
 24. Fan J, Hayes S, Freedman G, et al. Planning the Breast Boost: Dosimetric Comparison of CyberKnife, Photon Mini Tangents, IMRT, and Electron Techniques. *Int J Radiat Oncol Biol Phys.* 2010; 78(3): S788–S789, doi: [10.1016/j.ijrobp.2010.07.1826](https://doi.org/10.1016/j.ijrobp.2010.07.1826).
 25. Anbumani S, Palled SR, Prabhakar GS, et al. Accelerated partial breast irradiation using external beam radiotherapy-A feasibility study based on dosimetric analysis. *Rep Pract Oncol Radiother.* 2012; 17(4): 200–206, doi: [10.1016/j.rpor.2012.04.002](https://doi.org/10.1016/j.rpor.2012.04.002), indexed in Pubmed: [24377024](https://pubmed.ncbi.nlm.nih.gov/24377024/).
 26. Major T, Stelczar G, Pesznyák C, et al. Multicatheter interstitial brachytherapy versus intensity modulated external

- beam therapy for accelerated partial breast irradiation: A comparative treatment planning study with respect to dosimetry of organs at risk. *Radiother Oncol.* 2017; 122(1): 17–23, doi: [10.1016/j.radonc.2016.08.003](https://doi.org/10.1016/j.radonc.2016.08.003), indexed in Pubmed: [27544819](https://pubmed.ncbi.nlm.nih.gov/27544819/).
27. Charaghvandi RK, den Hartogh MD, van Ommen AMLN, et al. MRI-guided single fraction ablative radiotherapy for early-stage breast cancer: a brachytherapy versus volumetric modulated arc therapy dosimetry study. *Radiother Oncol.* 2015; 117(3): 477–482, doi: [10.1016/j.radonc.2015.09.023](https://doi.org/10.1016/j.radonc.2015.09.023), indexed in Pubmed: [26438972](https://pubmed.ncbi.nlm.nih.gov/26438972/).
 28. Fröhlich G, Mészáros N, Smanykó V, et al. Is stereotactic CyberKnife radiotherapy or multicatheter HDR brachytherapy the better option dosimetrically for accelerated partial breast irradiation? *Brachytherapy.* 2021; 20(2): 326–331, doi: [10.1016/j.brachy.2020.10.003](https://doi.org/10.1016/j.brachy.2020.10.003), indexed in Pubmed: [33221260](https://pubmed.ncbi.nlm.nih.gov/33221260/).
 29. Herein A, Stelczer G, Pesznyák C, et al. Multicatheter interstitial brachytherapy versus stereotactic radiotherapy with CyberKnife for accelerated partial breast irradiation: a comparative treatment planning study with respect to dosimetry of organs at risk. *Radiol Oncol.* 2021; 55(2): 229–239, doi: [10.2478/raon-2021-0016](https://doi.org/10.2478/raon-2021-0016), indexed in Pubmed: [33768766](https://pubmed.ncbi.nlm.nih.gov/33768766/).
 30. Nath R, Anderson LL, Luxton G, et al. Dosimetry of interstitial brachytherapy sources: recommendations of the AAPM Radiation Therapy Committee Task Group No. 43. *American Association of Physicists in Medicine. Med Phys.* 1995; 22(2): 209–234, doi: [10.1118/1.597458](https://doi.org/10.1118/1.597458), indexed in Pubmed: [7565352](https://pubmed.ncbi.nlm.nih.gov/7565352/).
 31. Mészáros N, Smanykó V, Major T, et al. Implementation of Stereotactic Accelerated Partial Breast Irradiation Using Cyber-Knife - Technical Considerations and Early Experiences of a Phase II Clinical Study. *Pathol Oncol Res.* 2020; 26(4): 2307–2313, doi: [10.1007/s12253-020-00821-3](https://doi.org/10.1007/s12253-020-00821-3), indexed in Pubmed: [32472440](https://pubmed.ncbi.nlm.nih.gov/32472440/).
 32. Baltas D, Kolotas C, Geramani K, et al. A conformal index (COIN) to evaluate implant quality and dose specification in brachytherapy. *Int J Radiat Oncol Biol Phys.* 1998; 40(2): 515–524, doi: [10.1016/s0360-3016\(97\)00732-3](https://doi.org/10.1016/s0360-3016(97)00732-3), indexed in Pubmed: [9457842](https://pubmed.ncbi.nlm.nih.gov/9457842/).
 33. Bondiau PY, Bahadoran P, Lallement M, et al. Robotic stereotactic radioablation concomitant with neoadjuvant chemotherapy for breast tumors. *Int J Radiat Oncol Biol Phys.* 2009; 75(4): 1041–1047, doi: [10.1016/j.ijrobp.2008.12.037](https://doi.org/10.1016/j.ijrobp.2008.12.037), indexed in Pubmed: [19386428](https://pubmed.ncbi.nlm.nih.gov/19386428/).
 34. Vermeulen S, Cotrutz C, Morris A, et al. Accelerated Partial Breast Irradiation: Using the CyberKnife as the Radiation Delivery Platform in the Treatment of Early Breast Cancer. *Front Oncol.* 2011; 1: 43, doi: [10.3389/fonc.2011.00043](https://doi.org/10.3389/fonc.2011.00043), indexed in Pubmed: [22649764](https://pubmed.ncbi.nlm.nih.gov/22649764/).
 35. Vermeulen SS, Haas JA. CyberKnife stereotactic body radiotherapy and CyberKnife accelerated partial breast irradiation for the treatment of early breast cancer. *Transl Cancer Res.* 2014; 3(4): 295–302, doi: [10.3978/j.issn.2218-676X.2014.07.06](https://doi.org/10.3978/j.issn.2218-676X.2014.07.06).
 36. Obayomi-Davies O, Kole TP, Oppong B, et al. Stereotactic Accelerated Partial Breast Irradiation for Early-Stage Breast Cancer: Rationale, Feasibility, and Early Experience Using the CyberKnife Radiosurgery Delivery Platform. *Front Oncol.* 2016; 6: 129, doi: [10.3389/fonc.2016.00129](https://doi.org/10.3389/fonc.2016.00129), indexed in Pubmed: [27242967](https://pubmed.ncbi.nlm.nih.gov/27242967/).
 37. Lozza L, Fariselli L, Sandri M, et al. Partial breast irradiation with CyberKnife after breast conserving surgery: a pilot study in early breast cancer. *Radiat Oncol.* 2018; 13(1): 49, doi: [10.1186/s13014-018-0991-4](https://doi.org/10.1186/s13014-018-0991-4), indexed in Pubmed: [29566762](https://pubmed.ncbi.nlm.nih.gov/29566762/).
 38. Weed DW, Edmundson GK, Vicini FA, et al. Accelerated partial breast irradiation: a dosimetric comparison of three different techniques. *Brachytherapy.* 2005; 4(2): 121–129, doi: [10.1016/j.brachy.2004.12.005](https://doi.org/10.1016/j.brachy.2004.12.005), indexed in Pubmed: [15893265](https://pubmed.ncbi.nlm.nih.gov/15893265/).