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# Brachytherapy boost in women with early-stage breast cancer treated with breast conserving therapy

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## Summary

In women with early stage breast cancer brachytherapy (BR) boost allows increase of the dose administered to the tumour bed, following whole-breast irradiation. In the present paper high-dose-rate and low-dose-rate brachytherapy results are presented, in comparison to external electron beam radiotherapy. Results of Phase II and III trials show that both techniques give comparable results regarding efficacy. In most patients satisfying cosmetic results can also be obtained, with acceptable local recurrence rate not exceeding 10%.

**Key words**

**brachytherapy • boost • breast cancer**

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The history of brachytherapy (BR) in Europe began in 1901, when the Head of the Dermatology Ward in St. Luis Hospital in Paris, Henry Alexander Danlos, used radium for the treatment of lupus erythematosus type skin malformation. He placed several milligrams of this radioactive element (borrowed from Marie and Pierre Curie) in a rubber tube directly on the skin of the patient [1]. In the years 1924–1929 the British surgeon Geoffrey Keynes treated 90 breast cancer patients using radium irradiation exclusively [2]. Nowadays, radiotherapy alone is used in patients with locally advanced breast cancer who do not accept surgical treatment or if contraindications to surgery are present. In those cases the whole breast is irradiated (50Gy external beam radiotherapy). BR is one of the methods allowing an increase of the dose delivered to the tumour [3,4]. BR alone is the treatment of choice in patients with locally recurrent breast cancer after breast conserving treatment (including radiotherapy), who refused mastectomy [5–7].

Breast conserving treatment is the treatment of choice in early cancer. Despite years of observation it is still regarded as controversial – not in regard to the very idea; the controversy pertains rather to the way it is being performed by radiotherapists and surgeons. There are no uniform indications as far as the optimal surgery range is concerned (lumpectomy alone, lumpectomy with the macroscopic margin of 1cm, excision of the breast tissue block of a segment or a quadrant).

Breast irradiation is an essential element of the conservative approach. Local recurrence risk after surgery alone reaches 35%, compared to 10% in patients undergoing adjuvant radiotherapy [8]. First, the whole breast is irradiated using external beam technique, usually with a dose of 50Gy. Subsequently it is necessary to increase the dose delivered to the tumour bed using a so-called “boost”. There is no generally accepted term for the boost in Polish radiological vocabulary. The authors of this article decided to use the term “dopromienianie”, proposed by Fijutha and Nagadowska in 1996 [9].

Primary boost dose methods include teleradiotherapy (TRT) with external photon or electron (usually) beam and high dose rate (HDR) or low dose rate (LDR) brachytherapy [10]. The main advantage of brachytherapy results from the possibility of delivering a high dose of radiation to a limited volume of tissue in a short time peri-

od. However, one must remember that if the implants are misplaced the high dose irradiation area may exceed the tumour bed. Also the radiobiological effects of significantly shorter irradiation time are not well known (current models of equivalent doses are not applicable to interstitial brachytherapy setting).

### **BRLDR VERSUS TRT**

The only study comparing efficacy of BRLDR to TRT of which results are available in the literature was conducted in the Curie Institute in Paris. Fourquet et al. studied a group of 255 breast cancer patients in clinical stages T2–T3, treated with irradiation alone. They showed that during the 5-year follow-up period the recurrence rate after the electron beam boost was 30% versus 16% ( $p=0.03$ ) in patients receiving the boost from an interstitial iridium 192 implant [3].

In Tables 1 and 2 the comparison of the efficacy results of these boost techniques is presented.

The dose of 0.40–0.60Gy /hour was used in all cases where BRLDR was applied.

The two methods show similar and comparable efficacy rates. However, it must be noted that the analysis was conducted retrospectively. Also, in some series in which interstitial boost was used, the mean age of patients was significantly lower than in the external beam group [11,13,15].

### **BRHDR VERSUS TRT**

In two studies the efficacy of BRHDR and TRT as a boost in non-advanced breast cancer patients with breast conserving treatment was compared. First, whole breast irradiation was performed using an external photon beam (50Gy in classical fractionation). Subsequently Hammer et al. delivered a boost to the tumour bed using either an electron beam (TRT-11Gy in 5 fractions) or BRHDR (single 10Gy boost). Local recurrence rates were 8.2% and 4.3% ( $p<0.04$ ), respectively. Excellent or good cosmetic results were achieved in 70% and 88%, respectively ( $p<0.0001$ ) [19]. Polgar et al., in a randomized clinical Phase III trial, after the first stage of the study randomized the patients into 2 groups. In the first group the patients received external electron beam therapy of 16Gy in 8 fractions. In the second group the same total dose was delivered in the form of BRHDR. Local recurrence rates were 6% and 8.5%, respectively. Excellent or good cosmetic

**Table 1.** Comparison of effectiveness of TRT (electrons) and BRLDR irradiation.

Author and publication date	Number of cases	Percentage of recurrence (%)		p
		TRT	BRLDR	
De la Rochefordiere et al. 1992 [11]	337	7	8	NS
Mansfield et al. 1995 [12]	1070	18	12	0.05
Touboul et al. 1995 [13]	329	8	5.5	NS
Perez et al. 1996 [14]	619	6	7	NS
Wazer et al. 1997 [15]	214	3	4	NS
Vicini et al. 1997 [16]	385	4	4	NS
Collette et al. 2000 [17]	5312	4.5	2.5	0.09
Berberich et al. 2002 [18]	229	1.5	5.0	NS

NS – not significant.

**Table 2.** Cosmetic effect depending on irradiation method.

Author and publication date	TRT		BRLDR		p
	DCD (Gy)	EKZD (%)	DCD (Gy)	EKZD (%)	
De la Rochefordiere et al. [11]	16	97	20	95	NS
Mansfield et al. [12]	20	95	20	91	NS
Touboul et al. [13]	15	83	20	62	0.001
Perez et al. [14]	10–20	81	10–20	75	NS
Wazer et al. [15]	20	68	20	90	0.001
Vicini et al. [16]	15	90	15	90	NS

DCD – total dose from irradiation.

**Table 3.** BRHDR method irradiation results.

Author and publication year	Number of cases	DCD (Gy)	Percentage of local recurrence	EKZD (%)
Hammer 1994 [19]	208	10	4.3	88
Perera 1995 [22]	39	37.2	2.6	95
Guix 2002 [23]	41	30	7.0	79
Polgar 2002 [20]	56	16	8.5	88
Keisch 2003 [24]	43	34	0.0	88
Kulik 2004 [21]	93	10	1.1	85

results were achieved in 83% and 88%, respectively [20]. The differences between rates in the two groups were not statistically significant. Kulik from the Oncology Centre in Warsaw presented the results of a high dose rate interstitial boost study in 93 patients undergoing conserva-

tive treatment. During the 3-year follow-up one case of local recurrence was observed; excellent or good cosmetic results were achieved in 85% of patients. In a ProRough rule induction analysis including all clinical and therapeutic variables it was shown that patients with a mammography

diameter of tumour not exceeding 11mm have the best chance of excellent or good cosmetic results [21].

The results of BRHDR boost therapy are shown in Table 3. In all series shown, the dose rate was above 12Gy/hour.

Reaching an unequivocal opinion on which of the two boost techniques, TRT or BRHDR, is more efficient is not an easy task. Results of the above-cited studies are inconsistent. Hammer et al. showed significantly lower local recurrence rates with significantly higher rate of excellent and good cosmetic results for the interstitial boost, while the group from the National Oncology Institute in Budapest did not confirm these results in the settings of a randomized study [19,20]. Irrespective of the dose rate (HDR or LDR) better cosmetic results by BR boost can be explained by the lower dose delivered to the skin. This results from the fact that the distance between the most "superficial" interstitial guide needle and the skin should reach 5mm. Thus the danger of teleangiectasias and fibrosis, which significantly influence cosmetic outcomes, is reduced. Due to the beam geometry this cannot be achieved using electron beam teletherapy [25].

Questions and doubts:

- How to precisely define the additionally irradiated area (CTV – clinical target volume), if there is no PTV (planning target volume) in interstitial brachytherapy [26]?
- What is the optimal safety margin for the target including the tumour bed – 10, 15 or 20 mm [10]?
- How to determine this margin in clinical practice? The most commonly used methods (leaving metal markers in the wall of the lumpectomy site or using ultrasonography) have an error margin of 30–50% [27–30].
- Are the methods of intraoperative brachytherapy applicator placement or intraoperative external beam irradiation therapy better, as far as the error margin in CTV determination is concerned [8,22]?
- Are the cosmetic effects in patients treated with intraoperative and postoperative brachytherapy comparable [31]?
- What irradiation methods are optimal for specific patient groups?

It seems that those questions could be answered by the results of Phase III study (studies?) conducted in comparable patients groups, with uniform inclusion, treatment indications and evalu-

ation criteria. It would enable boost procedures to be standardized in breast cancer patients undergoing conservative treatment.

## CONCLUSIONS

A boost delivered to the tumour bed in non-advanced breast cancer patients undergoing conservative treatment improves the local control results. The two currently used techniques of local dose increase – with either external electron beam therapy or interstitial high dose or low dose rate brachytherapy – give comparable results. In most patients a satisfying cosmetic result can be achieved, with a local recurrence rate not exceeding 10%.

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