World Journal of Breast Cancer Research

Research Article
Published: 10 Jan, 2018

Feasibility of Permanent Breast ^{103}Pd Seed Implant for Early Stage Breast Cancer

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Abstract

Background and Purpose: In order to improve the offer of care in our institution, the goal of this study was to evaluate the logistical feasibility of Permanent Breast Seed Implant (PBSI) with 103Pd in women with early stage breast cancer.

Material and Methods: From June 2014 to January 2016 eligibility criteria for PBSI were evaluated for all patients seen for breast cancer treatment after breast conserving surgery. After patient consent and acquisition of Ultra Sound (US) imaging, some patients were excluded based on the following morphological criteria: smaller breast, larger seroma, closer the skin or the chest wall.

Results: Among the 1,032 patients seen in consultation, 184 (17.8%) were eligible according to clinical and histological criteria. Ineligibility was mostly due to chemotherapy, tumor size, surgical margin, positive lymph node and multifocal disease. Of those patients, 100 were not informed of the study for various reasons: logistical issues such as technical availability, not enough consultation time, waiting for chemotherapy decision, uncertain diagnosis or oversight (45%), breast clinical morphology (18%), no radiation therapy (17%) and psychological disorders (14%). Among the 24 patients interested in PBSI, 19 were finally excluded after breast US imaging due to the seroma cavity dimension, the proximity of the chest wall or that of the skin surface.

Conclusion: The recruitment in the study was lower than expected mainly for logistical issues. We hope that our good preliminary results will convince our colleagues to present the technique to eligible patients in order to increase recruitment. This study shows the difficulty to introduce a new technique in a busy department.

Keywords: Brachytherapy; Breast cancer; Permanent seed implant; Feasibility; Logistic

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Received Date: *13 Sep 2017*
Accepted Date: *02 Jan 2018*
Published Date: *10 Jan 2018*

Citation:
Colliaux J, Vigneault E, Varfalvy N, Dagnault A. Feasibility of Permanent Breast ^{103}Pd Seed Implant for Early Stage Breast Cancer. World J Breast Cancer Res. 2018; 1(1): 1004.

Introduction

Adjuvant radiation treatment has become a standard after breast conserving surgery for breast cancer. It leads to good local control and the majority of local recurrences occur in close proximity to the tumour bed [1-3]. Many patients develop fatigue and acute skin reactions ranging from simple redness to painful skin break-down [4]. However, 15% to 30% of women treated with breast conserving surgery failed to receive whole breast irradiation due to patient inconvenience, physician preference, and logistical problems [5-7]. For several years, Accelerated Partial Breast Irradiation (APBI) has been increasingly used as an alternative to Whole Breast Irradiation (WBI). The development of APBI was initiated in order to decrease side effects (skin and cardiac toxicity, risk of induced secondary cancer) [8-10], patient logistics, and treatment cost [11]. Numerous APBI trials confirmed the significant impact of local dose on local control rates [12-16]. A number of experts groups have established guidelines to define eligibility criteria for partial breast irradiation [10,17-19].

Several APBI options exist including external beam radiation (using three-dimensional Conformal Radio Therapy (3D-CRT), Intensity Modulated Radiation Therapy (IMRT), proton radiation or intra operative radiation therapy) and brachytherapy (using either intracavitary or interstitial approaches).

A new Permanent Breast Seed Implant (PBSI) technique was pioneered in Canada by Pignol et al. [20-22] and allows for a single day treatment with good efficacy and safety. This technique consists of implanting preloaded needles of Palladium (^{103}Pd) seeds in the tumor bed to provide a dose of 90 Gy on the Planning Target volume (PTV).

In order to improve the offer of care in our institution, the goal of this study was to evaluate the

Table 1: Patients clinical and tumor characteristics.

Characteristic	Value
Age (y)	
Mean (SD)	60.5 (±10.9)
Range	23-91
T stage n (%)	
Tis	184 (15.0)
T1mic	2 (0.2)
T1a	73 (6.0)
T1b	172 (14.1)
T1c	363 (29.7)
T2	316 (25.8)
T3	76 (6.2)
T4a	5 (0.4)
T4b	13 (1.1)
T4c	1 (0.1)
T4d	11 (0.9)
Tx	7 (0.6)
Histopathologic Grade n (%)	
1	315/1223 (25.8)
2	558/1223 (45.6)
3	341/1223 (27.9)
Unknown	9/1223 (0.7)
ER status n (%)	
Estrogen receptor	
Positive	1042/1223 (85.2)
Unknown	11/1223 (0.9)
Progesterone receptor	
positive	931/1223 (76.1)
Unknown	12/1223 (1)

logistical feasibility of PBSI in women with early stage breast cancer.

Materials and Methods

Patients

Between June 2014 and January 2016, we have evaluated the eligibility criteria of all new patient consults with local breast cancer in our institution after breast conserving surgery. The criteria were chosen according to those recommended by GEC-ESTRO [17]. Women eligible for PBSI include individuals ≥ 50 years of age with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 who have undergone lumpectomy for unifocal infiltrating ductal carcinoma, positive or negative oestrogen and progesterone receptor, grade 1 cm, 2 cm or 3 cm, <3 cm in diameter, with surgical margins ≥ 2 mm, no lymphovascular invasion, no positive sentinel lymph node and a delay between surgery and radiation therapy <4 months. Lobular histologic features were allowed. Women with ductal carcinoma *in situ* only or histological features >25%, medical history of auto immune disease, cancer (except skin or T1 cervix cancer), BRCA 1/BRCA 2 mutation or insulin-dependent diabetes were considered ineligible. Women with an unhealed scar or on anticoagulant were not eligible. Eligibility was evaluated before the inclusion in the PBSI protocol. Eligible patients signed an informed consent. Patients' characteristics and eligibility criteria are reported in Table 1. Morphological criteria were evaluated on CT-scan simulation and breast Ultra Sound (US). This study has been approved by the institution Ethic Review Board.

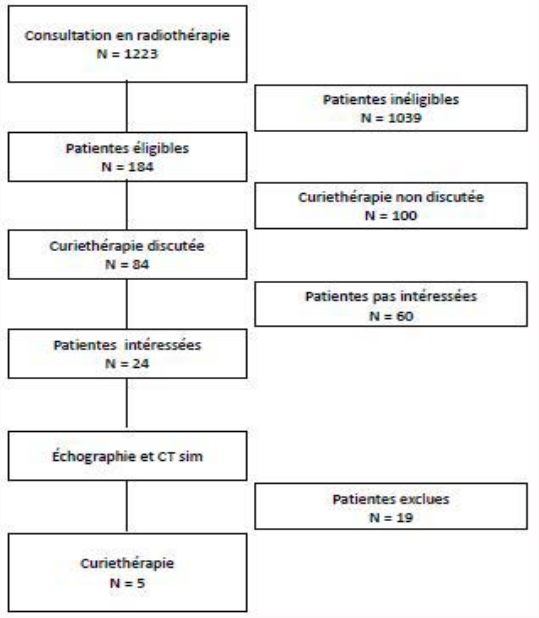

Figure 1: Flow Chart.

Planning process

The planning process was adapted from Pignol's experience [20-23]. First, the CT-scan simulation was performed in the same condition as those of external beam radiation therapy, the patient lying supine on the table with arms lifted above their head. A slice thickness of 2 mm or 3 mm was selected. The isocenter was marked with skin tattoos. Then, the breast US was performed to localize and measure the size of the surgical bed and to evaluate its distance to the skin surface and the chest wall. Patients were excluded if they presented with a seroma larger than ≥ 2.5 cm in length in 2 directions, close the skin surface (<5 mm) or the chest wall (<8 mm) or if the tumor bed was localized too far in the inner quadrant of the breast (making it more difficult to reach the cavity with implantation needles).

Results

Patients

From July 2014 to January 2016, 1,032 consecutive new consult patients with local breast cancer were seen in our department after breast conserving surgery. Characteristics of patients are summarized in Table 1 and the flow chart of this study is shown on Figure 1.

After a first screening, only 184 patients (17.8%) were potentially eligible for PBSI according to their clinical and histological tumor characteristics. The main reasons of ineligibility were chemotherapy (29.2%), tumor size of more than 3 cm (25.7%), and surgical margin of less than 2 mm (27.9%), positive sentinel lymph node biopsy (21.1%) and multicentric or multifocal tumor (19.4%), as shown in Table 2.

Among those eligible, only 84 received information about the PBSI. The various reasons for not offering the PBSI protocol to eligible patients are shown in Figure 2. In 45% of cases, the information wasn't given for logistical issues such as technical availability for 24 patients (lack of clinical staff : anaesthetist, physicist or physician), because of

Table 2: Eligibility and ineligibility criteria.

		YES n (%)	NO n (%)
ELIGIBILITY	Patients ≥ 50 years old	1071 (87.6)	152 (12.4)
	Performance status ECOG 0 or 1	1217 (99.5)	6 (0.0)
	Breast conserving surgery	1032 (84.4)	191 (15.6)
	Tumor size of invasive ductal carcinoma <3 cm	834 (68.2)	389 (31.8)
	Surgical margins ≥ 2 mm	861 (70.4)	359 (29.4)
	Negative sentinel lymph node biopsy	868 (71.0)	351 (28.7)
	Lymphovascular infiltration	927 (75.8)	233 (19.1)
	Timeout after surgery <4 months	1109 (90.7)	114 (9.3)
INELIGIBILITY	Multicentric or multifocal tumor	283 (23.1)	940 (76.9)
	BRCA 1/BRCA 2 mutation	7 (0.1)	1216 (99.4)
	Extensive in situ carcinoma	66 (5.4)	1156 (94.5)
	Pure ductal carcinoma *in situ*	178 (14.6)	1044 (85.4)
	Chemotherapy	452 (37.0)	771 (63.0)
	Prior history of cancer (except skin or T1 cervix cancer)	78 (6.4)	1145 (93.6)
	Auto immune disorder	37 (3.0)	1186 (97.0)
	Insulin-dependent diabetes	7 (0.1)	1216 (99.4)
	Breast implants	29 (2.4)	1194 (97.6)
	Scar skin infected or not completed	72 (5.9)	1151 (94.1)
	Treatment of anticoagulant	75 (6.1)	1148 (93.9)

too short consultation time for 5 patients, waiting for chemotherapy decision for 7 patients, forgot to talk about for 2 patients or uncertain diagnosis for 7 patients. The 18% breast clinical morphology issues included breast and seroma size (4 and 6 patients) and seroma location (8 patients). Seventeen percent decided not to be treated by radiation therapy for observation and 14% had some psychological disorders like anxiety or psychiatric disease. 60 patients did not consent to be treated by PBSI after being given the information. After screening with the initial consultation, 24 patients were interested in the PBSI. Then, the breast US and the CT-scan simulation were scheduled to check the localization and size of the seroma cavity. After this evaluation, 19 patients were excluded. Some because of a seroma cavity larger than 2.5 cm in diameter (15 patients), some because the chest wall was too close (5 patients), some because the skin surface was too close (5 patients), because of technical availability (2 patients) and one because a seroma location. The majority of excluded patients had more than one reasons to be excluded.

Finally, 5 patients were selected to be treated with PBSI.

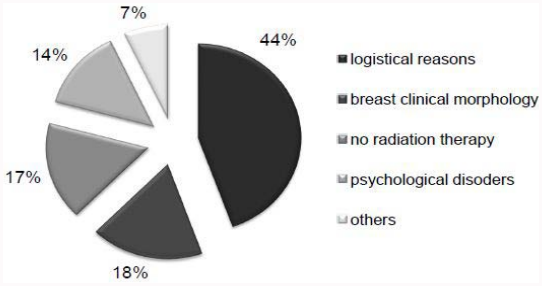

Figure 2: Reasons of non-information about permanent breast seed implantation for eligible patients.

Discussion

Pignol and colleagues have developed a low-dose-rate permanent breast seed implant brachytherapy technique for partial-breast irradiation [20]. They published encouraging results from the procedure, achieving successful PTV coverage, minimal skin toxicity, excellent patient satisfaction with no significant risk of local recurrence over a median follow-up period of 63 months for 134 patients [21]. Given these results and the convenience of a single day treatment, PBSI is an attractive treatment option for early-stage breast cancer patients.

In our study, the characteristics of all patients seen during the time of analysis were similar to those found in the literature: mean age of 60.9 years, the majority of tumor dimensions between 1 cm and 3 cm and positive hormonal receptors.

At the first screening, the reasons for ineligibility were: tumor size, surgical margins and positive sentinel lymph node. Surgical margins in our institution are often tight. The most frequent criteria of ineligibility were chemotherapy, multicentric or multifocal tumor and Ductal Carcinoma *In Situ* (DCIS). The ratio of eligibility in our population was 17.8% before morphological evaluation. At the time of analysis, we observed a low ratio of modified radical mastectomy with 191 patients who were not included in the 1,032 patients. Consequently, the number of patients with locally advanced breast cancer treated by chemotherapy, after or before breast conserving surgery, was higher than other series. Therefore, the high proportion of chemotherapy and surgical margin <2 mm could explain this low ratio of eligibility. Some studies included DCIS for the PBSI treatment. In the future, recruitment could be improved by including DCIS with low risk as RTOG 9804 criteria [24]. Another difficulty was to inform and recruit APBI eligible patients. Only 45% of eligible patients (84/184) were made aware and informed of the PBSI treatment. Among non-informed eligible patients, 49 were non-suitable for this technique because they had at least one psychological disorder,

they did not want radiation therapy or clinical morphological criteria were not good. Although, 45 patients were not informed due to logistical reasons, the logistical situation could improve in the future. Sometimes, delays to inform patients were due to unavailable oncotype DX results (needed to decide on chemotherapy). Then, among informed patients 71.4% (60/84 patients) were not interested. That could be improved by implication of all physicians to develop PBSI in our department, reassuring patients about the quality and safety of this treatment. The reasons for this patient aversion to the PBSI were not always explained. It can be assumed that at least some of them were uneasy about having permanent radioactive material in their body. The necessity of another general anaesthesia could also have been a deterrent and some might simply not generally be inclined to participate in a novel technique. Of the patients from which consent was obtained only 21% (5/24patients) were still eligible for PBSI compared to 55% in the Pignol series [25]. We were more stringent in our patient selection to facilitate the development of this new technique in our center. It is interesting to note that this study is the first one which talks about patients' recruitment in case of PBSI.

Conclusion

The recruitment of patients was lower than expected mainly for logistical issues. We hope that our good preliminary results will increase recruitment. This study shows the difficulty to introduce a new technique in a busy department.

Acknowledgement

Ghyslain Leclerc and Luc Beaulieu for writing assistance, Jean Philippe Pignol for help to develop the PBSI in our department, Isabelle Germain, Valérie Théberge, Nathalie Lessard, Lucie Blondeau for recruiting patients and Fondation du Cancer du sein de Québec for its sources of funding.

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