

TARGETED INTRAOPERATIVE RADIOTHERAPY WITH INTRABEAM SYSTEM: THE NOVEL APPROACH FOR BREAST CANCER TREATMENT IN VIETNAM

Nguyen Dinh Tung¹, Pham Nhu Hiep¹, Nguyen Viet Dung¹,
Nguyen Van Phuc¹, Nguyen Tuu¹, Tran Van Thanh¹,
Nguyen Huu Minh Tuan¹, Nguyen Cao Dung¹

ABSTRACT

Objective: The Oncology Center- Hue Central Hospital introduced 25 breast cancer cases in stage I, II that was treated by breast conserving therapy and nipple sparing mastectomy following targeted intraoperative radiotherapy with Intrabeam system.

Methods: It provided a point source of low energy from 16 to 20 Gy for breast conserving surgery and 10-12Gy for nipple sparing mastectomy. The applicator was inserted inside the bed tumor after removing tumor or retroaerolar tissue after mastectomy. This novel approach required the combination of several physicians: physic engineer, technician, radiation oncologist, surgeon, pathologist, anesthesiologist ...

Results: There is 22/25 cases for breast conserving therapy and 3/25 cases indicated nipple sparing mastectomy, 19/25 patients using single dose, 6/25 patients has boost and whole breast external beam radiation therapy. The first result obtained the safety in procedure and decreasing the hospitalisation for the whole breast radiation. Follow up time 20 months, there is no local recurrence, no distance metastasis, no necrosis the nipple aerolar complex, 14/25 cases gained good cosmetic results, most of them was feeling happy and believing for this procedure.

Conclusion: The novel approach is opening the new direction for early breast cancer treatment in Vietnam.

I. BACKGROUND

Breast cancer is the leading cancer in Vietnamese women. The ASR of this disease is 30/100.000 inhabitant in Hanoi and 20.1/100.000 in Hue. Globocan predicted that there will be 12.125 new cases and 5215 cases died from breast cancer in Vietnam in 2015.

Lumpectomy and radiation for whole breast is the standard treatment of breast cancer in the early stage.

Adjuvant whole-breast external beam radiotherapy (EBRT) is deemed mandatory after lumpectomy for breast cancer on the basis of the reduction of local recurrence in the conserved breast and of breast cancer mortality.

The clinicopathological paradox that led to the idea of focusing radiation to the tumour bed was motivated by the repeated observation that although two-thirds of specimens of mastectomies undertaken for small breast cancers harbor occult

1. Oncology Centre- Hue Central Hospital

Corresponding author: Nguyen Dinh Tung

Email: tung.phd@gmail.com

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cancer foci distributed throughout the breast most local recurrences in the conserved breast appear in the original tumour bed. We recognised that IORT by Intrabeam system would be a procedure targeted radiation into the bed of tumour after it was being removed. This procedure becomes popular in many country in the world.

Hue Central Hospital is one of three biggest hospital in Vietnam has received the improvement project for Cancer Center by medical equipments, we conducted this study to assess the first using intraoperative radiotherapy for Vietnamese breast cancer patients with early stage.

II. METHODS

The Intrabeam device (Carl Zeiss Meditec, Oberkochen, Germany) provides a point source of 50 kV energy x-rays at the centre of a spherical applicator. The appropriately sized (1.5-5.0 cm diameter) applicator is placed in the tumour bed using a meticulous surgical technique, including a carefully inserted purse-string suture that ensures that breast tissues at risk of local recurrence receive the prescribed dose while skin and deeper structures are protected. Radiation is delivered over 20-45 min to the tumour bed. The surface of the tumour bed typically receives 20 Gy that attenuates to 5-7 Gy at 1 cm depth.

This technique employs a miniature electron-beam driven X-ray source that emits soft X-ray (50kV) from within the breast. There is a quick attenuation of the radiation within tissues so that the dose is inversely proportional to the third power of the distance and this reduces the damage to surrounding normal tissues and minimizes the need for radiation protection to the operating personnel.

The diameter of the cavity is measured with a disposable tape measure cut to 4cm or 5cm. This and the judgement of how well the breast wraps around the applicator - actually inserting the applicators in the wound and visualizing the apposition is very useful - will determine the size of the applicator. The usual size of applicator is from 3,5, 4,0 or 4,5cm. We have used the 3 or 5cm applicators only a few times.

If the tumor is on the left side, a tungsten-impregnated rubber shield is used to cap the applicator, to protect the heart and coronary vessels.

In process of delivery radiation, patient have to spend in the operation room under control of anesthesia.

III. RESULTS

3.1 General Characteristics

Characteristics	N.of patient
Age	45-79
Untrasound	malignant : 9/25
Mammography	malignant : 11/25 Calcification : 6/25
Tumour size	< 2cm : 15 2-3cm : 10
Clinical Node	No : 23/25 N1 : 2/25
Pathology	Ductal : 23/25 Mucinous : 02/25
Grade	Grade 1: 7/12 Grade 2: 18/25
Hormone receptor	ER (+)/PR(+): 17/25 ER (+)/PR(-): 8/25 Her2Neu(+): 5/15

3.2. Characteristics of intraoperative radiotherapy with Intrabeam system :

Characteristics	N. of patient
Procedure	Conservation Therapy 22/25 Nipple Sparing Mastectomy : 3/25
Applicator size	2,5cm: 1/25 3,0cm : 2/25 4cm : 5/25 4,5cm : 11/25 5cm : 6/25
Dose	10Gy : 3/25 (single dose for mastectomy) 14Gy : 2/25 16Gy : 4/25 20Gy : 16/25 (Single dose for conservation therapy)
Time	11-42 minutes

3.3. Follow up

Characteristics	N.of patient
Time of post-op	7 days : 16/25 > 7 days: 9/25
Complication	Cellulitis + bruising : 1/25 Erythema, fibrosis : 3/25
EBRT	6/25
Chemotherapy + Hormonotherapy	12/25
Oncology result	Recurrence : 0/25 Distant metastasis : 0/25
Cosmetic result	Good : 14/25

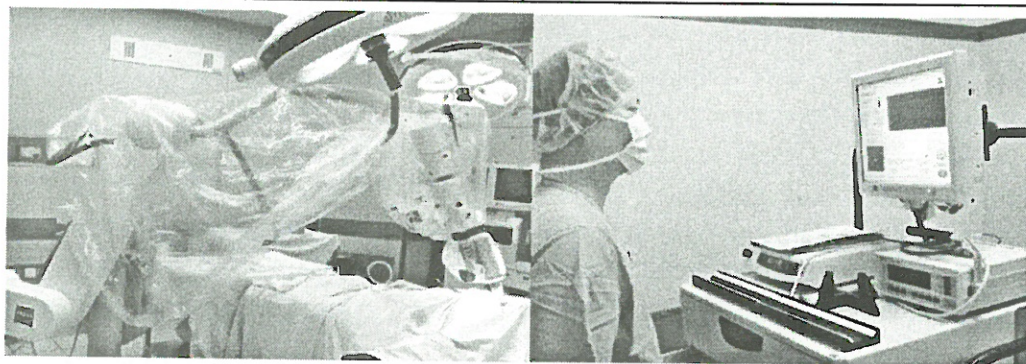


Fig 1 : Patient and IORT with Intrabeam system in the operative room

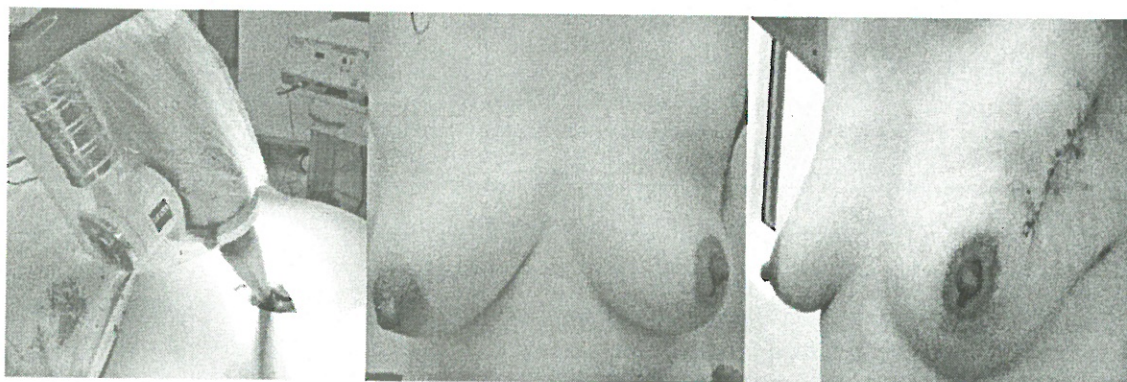


Fig 2 : IORT for breast conserving surgery

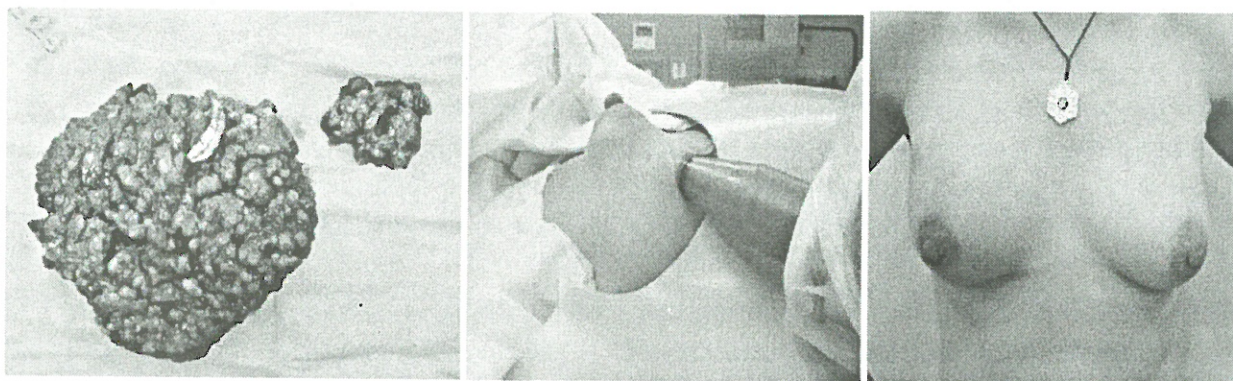


Fig 3: IORT for nipple sparing mastectomy and immediately breast reconstruction

IV. DISCUSSION

After breast-conserving surgery, 90% of local recurrences occur within the index quadrant despite the presence of multicentric cancers elsewhere in the breast. Thus, restriction of radiation therapy to the tumour bed during surgery might be adequate for selected patients. We compared targeted intraoperative radiotherapy with the conventional policy of whole breast external beam radiotherapy.

In this research, we selected the patient so favorable prognosis: Age over 45, tumour size was under 3cm, no palpable lymph node in clinical, most of them had the hormone receptor with ER, PR positive. This patient group is the same group in Singapore. TARGIT was performed in the similar characteristics but tumour size is under 3.5cm.

This investigator-initiated trial was launched in March, 2000, and reached the original accrual goal of 2232 participants in April, 2010. In July, 2010, when we reported the initial results for local control and early complications, the 4-year Kaplan-Meier estimate of local recurrence in the conserved breast was 1.20% (95% CI 0.53-2.71) for those randomised to TARGIT and 0.95% (0.39-2.31) for those randomised to EBRT.

Results of this research shown that the procedure of IORT was safe and effective. The complication was not remarkable and there was no patient who had occurred the local recurrence or distant metastasis in 20 months follow-up.

This procedure requires the cooperation between surgeons, radiation oncologists, medical physicists and other members of the multidisciplinary team. As the success of this technique depends on multidisciplinary team working harmoniously with each other and not individuals.

The randomised trials of external partial breast irradiation have not shown this technique to be an effective form of local control. A third

trial with a strict selection of patients, reported non-inferiority between partial and whole breast irradiation in terms of local control and survival after a median follow up of 10 years. A meta-analysis of partial breast irradiation showed an increased risk for both local and regional recurrence with partial breast irradiation, with no survival difference, when compared with whole breast irradiation.

We have 19/25 patient used a single dose for treatment. for this dose, patient have saving 4-6 weeks treatment comparing the whole breast -ERBT. Several investigators shown that IORT single-dose intraoperative radiation therapy was the dominant, more cost-effective strategy, providing greater quality-adjusted life years at a decreased cost compared with 6-week WB-EBRT. With less cost and greater QALYs than WB-EBRT, IORT is the more valuable strategy. IORT offers a unique example of new technology that is less costly than the current standard of care option but offers similar efficacy.

We have 3 patients who was being used IORT by 10-12 Gy to preserve the nipple in the nipple sparing mastectomy and immediately breast reconstruction by implant. These patients was so happy for this procedure after 4 weeks. From December 2012 to June 2013, Pan L studied 7 female patients with breast cancer were enrolled in the study. nipple sparing mastectomy with or without axillary dissection was performed first. After confirming negative retroareolar frozen section results and no poor local bleeding in the nipple areolar complex, Intrabeam IORT was carried out with a single dose of 16 Gy, followed by breast reconstruction. Intrabeam IORT may be a feasible and convenient approach for NSM with breast reconstruction in patients with breast cancer.

V. CONCLUSION

The novel approach is opening the new direction for early breast cancer treatment in Vietnam.

REFERENCE

1. Alvarado (2013): Cost-effectiveness analysis of intraoperative radiation therapy for early-stage breast cancer. *Ann Surg Oncol.*; 20(9): pp.2873-80
2. Jayant S Vaidya (2010): Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial *The Lancet* 2010, Volume 376, Issue 9735, pp. 91 - 102.
3. Jayant S Vaidya (2013): Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial, *The Lancet*, Volume 383, Issue 9917, pp. 603 - 613
4. Pan L (2014): A Novel Approach of INTRABEAM Intraoperative Radiotherapy for Nipple-Sparing Mastectomy With Breast Reconstruction, *Clin Breast Cancer*. S1526-8209(14)00083-4.
5. Norman R. Williams (2014); Intraoperative radiotherapy for breast cancer *Gland Surg* ; 3(2): pp.109–119.
6. Tung D.N (2012): Breast cancer surgery in Vietnam, *Journal of breast cancer*, Vol 15: pp.155
7. Tung D.N, Hiep N. P & al (2013): First result of using targeted intraoperative radiotherapy (Intrabeam) for breast cancer, *Journal of Clinical Medicine* , Vol 17, pp.161-165.