高雄榮民總醫院

乳癌治療團隊

Principle of accelerative partial breast irradiation (APBI) with interstitial brachytherapy (ISBT) for early stage breast cancer

Kaohsiung VGH version 1.0, 2017

Indication:

Early stage breast carcinoma and low risk loco-regional recurrence

Low risk ductal carcinoma in situ

Patient selection and inclusion criteria:

1. Age: old than 50 y/o
2. Histology: invasive ductal, mucinous, medullary, colloid carcinoma Image appearance: unifocal
3. Tumor size: < 2cm
4. Margin: free
5. Lymph node status: pN0 (SLNB)
6. Hormone status: any, favor ER positive
7. Ductal carcinoma in situ
   (1) Screen detected
   (2) Low to intermediate nuclear grade
   (3) Size ≦ 2.5cm
   (4) Receted with margins negative ≧ 3mm

Exclusion criteria:

1. Age: < 30 y/o
2. Margin: positive
3. > 3cm ductal carcinoma in situ
4. Lympho-vascular invasion (LVI): not allowed (ESTRO & ASTRO)
5. Metastatic disease

Interstitial brachytherapy (ISBT) treatment procedures:

1. Patient selection in GS OPD
2. Radiation oncology OPD for 2nd discussion
3. Arrange operation date, announce Radiation oncology staff for scheduling
4. Lumpectomy and sentinel lymph node biopsy (SLNB)
5. Call radiation oncologist and waiting for the results of frozen section
6. If fulfilled the selection criteria, go on ISBT procedures. If not fulfilled the selection criteria, stop further procedures.
7. If final pathological report did not compatible with the selection criteria, adjuvant external beam radiotherapy (EBRT) for chest wall with or without regional lymphatic region should be arranged.

ISBT treatment technique and dosage protocol:

0.0 Evaluate the lumpectomy cavity status by CT scan before ISBT (optional).

1. Evaluate the size of lumpectomy cavity: selection of proper numbers of planes for insertion of the needles and catheters, ex. two to five planes.
2. Evaluate the depth of lumpectomy cavity: by ultra-sonography or x-rays
3. Placement of catheters: using breast template as guiding tool, insert the lead needles first, then replace these lead needles by treatment catheters.
4. Re-evaluate the placement of all catheters: by ultra-sonography or x-rays
5. Define the clinical target volume (CTV) by CT simulation
6. Dose calculation: 3D brachytherapy treatment planning system
6. Dosage: 28 Gy / 4 fractions or 36.4 Gy / 7 fractions or 32 Gy/8 fractions (Appendix)
7. Removal of the catheters after completion of the treatment

Follow-up:

- Oncology survey: as regular schedule
- Evaluation of cosmetic results: Fibrosis & skin atrophy etc by CTC AE v4.0

Reference:

1. Genebes C, Chand ME, Gal J, Gautier M, Raoust I, Ihrai T, Courdi A, Ferrero JM, Peyrottes I, Hannoun-Levi JM[1]. Accelerated partial breast irradiation in the elderly: 5-year results of high-dose rate multi-catheter brachytherapy. Radiat Oncol. 2014 May 16;9:115. doi: 10.1186/1748-717X-9-115.

2. Daya Nand Sharma, SVS Deo, Goura Kisor Rath, Nootan Kumar Shukla, Sanjay Thulkar, Renu Madan, and Pramod Kumar Julka. Perioperative high-dose-rate

interstitial brachytherapy boost for patients with early breast cancer. Tumori 2013;99(5):604-610
3. Strnad V, Hildebrandt G, Pötter R, Hammer J, Hindemith M, Resch A, Spiegl K, Lotter M, Uter W, Bani M, Kortmann RD, Beckmann MW, Fietkau R, Ott OJ. Accelerated partial breast irradiation: 5-year results of the German-Austrian multicenter phase II trial using interstitial multicatheter brachytherapy alone after breast-conserving surgery. Int J Radiat Oncol Biol Phys. 2011 May 1;80(1):17-24.
4. Resch A, Potter R, van Limbergen E, Biber E, Klein T, Fellner C, Handl-Zeller L, Langbauer G, Schürer-Waldheim H, Staffen A, Jakesz R, Kubista E, Lehr S, Seitz W: Long-term results (10 years) of intensive breast conserving therapy including a high-dose and large-volume interstitial brachytherapy boost (LDR/HDR) for T1/T2 breast cancer. Radiother Oncol, 63: 47-58, 2002.
5. Sperk E[1], Astor D, Keller A, Welzel G, Gerhardt A, Tuschy B, Sütterlin M, Wenz F. A cohort analysis to identify eligible patients for intraoperative radiotherapy (IORT) of early breast cancer. Radiat Oncol. 2014 Jul 12;9:154.

6. Njeh CF[1], Saunders MW, Langton CM. Accelerated Partial Breast Irradiation (APBI): A review of available techniques. Radiat Oncol. 2010 Oct 4;5:90.

7. Smith BD[1], Arthur DW, Buchholz TA, Haffty BG, Hahn CA, Hardenbergh PH, Julian TB, Marks LB, Todor DA, Vicini FA, Whelan TJ, White J, Wo JY, Harris JR. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 4, pp. 987–1001, 2009

8. Polgár C, Van Limbergen E, Pötter R Kovács G, Polo A, Lyczek J, Hildebrandt G, Niehoff P, Guinot JL, Guedea F, Johansson B, Ott OJ, Major T, Strnad V; 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 Mar;94(3):264-73.

9. Liu WS, Yen SH, Chang CH, Yang KM, Wu YP, Chen KY. Determination of the Appropriate Fraction Number and Size of the HDR Brachytherapy for Cervical Cancer. Gynecologic Oncology 1996: 60: 295–300.

10. Van der Kogel A, Joiner M Editor, Chapter 9. The linear quadratic approach in clinical practice. Basic Clinical Radiobiology, 4th Edition, 2009, Hodder Arnold Inc.

11. Candace Correa MD , Eleanor E. Harris MD, Maria Cristina Leonardi MD, Benjamin D. Smith MD, Alphonse G. Taghian MD PhD, Alastair M. Thompson MD, Julia White MD, Jay R. Harris MD. Accelerated Partial Breast Irradiation: Executive summary for the update of an ASTRO EvidenceBased Consensus Statement. Practical Radiation Oncology (2016)

Appendix 1: Calculation of the biological equivalent dose for tumor control

1. The α /β ratio of breast tumor is about 4.6 Gy, calculated from clinical results.
2. BED consideration:
   (1) EBRT: WB 45~50 Gy + 10 Gy boost, BED are 66~71.7 Gy for WB and 80~86 Gy with boost treatment
   (2) EBRT APBI: partial breast irradiation 38.5 Gy/10 fxs, BED 70 Gy
   (3) PDR ISBT: 50 Gy, 0.6 Gy/hr, BED 71.7 Gy
   (4) IORT: 20 Gy/1 fx, BED 107 Gy at surface, 64 Gy at 15 Gy isodose volume
   (5) HDR ISBT: 34 Gy/10 fxs BED 59 Gy or 36.4 Gy/7 fxs BED 77.5 Gy (France)
   Germen-Austrian: 32 Gy/8 fxs, BED 59.8 Gy
   28 Gy/ 4 fxs BED at 70.6 Gy (high dose region 125% with BED at 101.6 Gy)

Appendix 2: Calculation of the biological equivalent dose for acute and late tissue reactions

Table 9.1 Fractionation sensitivity of human normal tissues and tumours

Tissue/organ	Endpoint	α/β (Gy)	95% CL (Gy)	Source
Early reactions				
Skin	Erythema	8.8	6.9; 11.6	Turesson and Thames (1989)
	Erythema	12.3	1.8; 22.8	Bentzen *et al.* (1988)
	Dry desquamation	~8	N/A	Chogule and Supe (1993)
	Desquamation	11.2	8.5; 17.6	Turesson and Thames (1989)
Oral mucosa	Mucositis	9.3	5.8; 17.9	Denham *et al.* (1995)
	Mucositis	15	−15; 45	Rezvani *et al.* (1991)
	Mucositis	~8	N/A	Chogule and Supe (1993)
Late reactions				
Skin/vasculature	Telangiectasia	2.8	1.7; 3.8	Turesson and Thames (1989)
	Telangiectasia	2.6	2.2; 3.3	Bentzen *et al.* (1990)
	Telangiectasia	2.8	−0.1; 8.1	Bentzen and Overgaard (1991)
Subcutis	Fibrosis	1.7	0.6; 2.6	Bentzen and Overgaard (1991)
Breast	Cosmetic change in appearance	3.4	2.3; 4.5	START Trialists Group (2008)
	Induration (fibrosis)	3.1	1.8; 4.4	Yarnold *et al.* (2005)
Muscle/vasculature/ cartilage	Impaired shoulder movement	3.5	0.7; 6.2	Bentzen *et al.* (1989)

* This table was borrowed from the textbook of Basic Clinical Radiobiology, 4th Ed., Chapter 9, Hodder Arnold Inc., 2009.

Acute reaction: erythematous change α /β ratio = 8~8.8 Gy

1. EBRT: 60 Gy/30 fx, BED = 73.5~75 Gy
2. EBRT APBI: 38.5 Gy/10 fxs, BED = 55~57 Gy
3. IORT: 20 Gy/1 fx, BED = 48~58 Gy

4. HDR ISBT: 34 Gy/10 fxs, BED = 48.5 Gy; 36.4 Gy/7 fxs, BED = 60 Gy; 32 Gy/8 fxs, BED = 48 Gy
5. 28 Gy/ 4 fxs, BED = 42~47.5 Gy

Late reaction: cosmetic, α /β ratio 3.4 Gy from START Trials, fibrosis 3.1 Gy

1. EBRT: 60 Gy/30 fx, BED = 90.5~93.8 Gy
2. EBRT APBI: 38.5 Gy/10 fxs, BED = 55~57 Gy
3. IORT: 20 Gy/1 fx, BED = 113~122 Gy (90% prescription dose)
4. HDR ISBT(100% prescription dose): 34 Gy/10 fxs, BED = 68~71.6 Gy; 36.4 Gy/7 fxs, BED = 92~97.5 Gy; 32 Gy/8 fxs, BED = 69.6 ~ 73.2 Gy
   28 Gy/ 4 fxs, BED = 85.6~91.25 Gy

Appendix 3: Summary of BED calculation of tumor and tissue reactions

Table 1. The BED of tumor control and tissue reactions among different methods

Methods	Tumor control (BED, Gy)	Acute, erythema (BED, Gy)	Late, cosmetic (BED, Gy)
	α /β 4.6 Gy	α /β 8 ~ 8.8 Gy	α /β 3.1 ~ 3.4 Gy
EBRT, 60 Gy/30fxs	80~86	73~75	90~94
EBRT, 50 Gy/25fxs	66~72	62~63	79~82
EBRT, 38.5 Gy/10fxs	70	55~57	55~57
IORT, 20 Gy/1fx (80% isodose)	72	48~58	91~99
ISBT (from historical data)	59 to 78	<60	<98
34 Gy/10 fxs	59	47~49	68~72
36.4 Gy/7 fxs	78	58~60	92~98
32 Gy/8 fxs	60	47~48	70~73
28 Gy/4 fxs	71	42~48	86~91

Abbreviations: BED – biological equivalent dose, EBRT - external beam radiotherapy, IORT - intraoperative radiotherapy, ISBT - interstitial brachytherapy