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Irradiazione Parziale Accelerata della Mammella (APBI) con brachiterapia interstiziale HDR come secondo trattamento conservativo per recidiva mammaria/secondo tumore ipsilaterale

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CONSERVATIVE TREATMENT OF CANCER OF THE BREAST

BY
GEOFFREY KEYNES, M.A., M.D.(Camb.), F.R.C.S.

Assistant Surgeon, St. Bartholomew's Hospital; Surgeon, New Cross Hospital, Northwood
(With Sixteen Plates)

It is now nearly fifty years since William Stewart Halsted of Baltimore introduced the radical operation for the treatment of cancer of the breast. The technique of the operation has undergone modification during that period, but Halsted's principle has been accepted and his method of operation has been widely used. I believe that the patient would do just as well if only a local removal of the breast were performed. I must confess that my opinion has now gone to the opposite extreme, and I am prepared to maintain that if the axillary lymph nodes are extensively infested dissemination of the cells may be harmful and that if

Geoffrey Keynes nel 1937, eseguì 325
impianti mammari, con aghi di
Radium, ed ottenne una sopravvivenza
a 5 anni statisticamente equivalente
a quella della mastectomia radicale
Le sue pazienti, inoltre, evitarono
il linfedema associato alla
dissezione ascellare con migliori
esiti cosmetici



Breast Brachytherapy

- È la migliore modalità di RT conformazionale per coprire omogeneamente la cavità chirurgica con un margine di 1-2 cm
- Riduce la dose integrale parenchima mammario non interessato
- Somministra una dose tumoricida pari a quella della RT convenzionale post-chirurgia
- Eroga una dose omogenea
 - Ottimizza gli esiti cosmetici
 - Riduce la fibrosi e la steatonecrosi

Breast Brachytherapy

Benefits

- APBI riduce il tempo di trattamento da 6 settimane a 4 – 5 giorni
- Permette una erogazione e una distribuzione di dose costante e riproducibile
- Riduce la dose al cuore ed al polmone
- Riduce la dose \Rightarrow le reazioni cutanee nelle pazienti con mammelle di grossa taglia

In caso di IBTR (Ipsilateral Breast Tumour Recurrence) dopo terapia conservativa mammaria, la mastectomia radicale è attualmente considerata il gold-standard; ma nelle ultime due decadi, dopo IBRT, spesso, la sola terapia proposta è stata un 2° intervento conservativo

- Kurtz JM, et al. Results of wide excision for mammary recurrence after breast-conserving therapy. *Cancer* 61:1969-72; 1988
- Kurtz JM, et al. Is breast conservation after local recurrence feasible? *Eur J Cancer* 27:240-4; 1991
- Abner AL, et al. Prognosis following salvage mastectomy for recurrence in the breast after conservative surgery and radiation therapy for early-stage breast cancer. *J Clin Oncol* 11:44-8; 1993
- Dalberg K, et al. Outcome of treatment for ipsilateral breast tumor recurrence in early-stage breast cancer. *Breast Cancer Res Treat* 49:69-78; 1998
- Salvadori B, et al. Reoperation for locally recurrent breast cancer in patients previously treated with conservative surgery. *Br J Surg* 86:84-7; 1999
- Alpert TE, et al. Ipsilateral breast tumor recurrence after breast conservation therapy: outcomes of salvage mastectomy vs. salvage breast-conserving surgery and prognostic factors for salvage breast preservation. *Int J Radiat Oncol Biol Phys* 63:845-51; 2005
- Ichitani M, et al. Repeat lumpectomy for ipsilateral breast tumor

MCB as a 2nd Conservative Treatment

*La percentuale di
recidive locali (2°
LR) dopo
chirurgia
conservativa
esclusiva si
attesta intorno al
20%.*

*Al fine di ridurre
queste
percentuali è
stata proposta la
re-irradiazione
con BT
interstiziale multi-
catodora*

*Crescente ed accattivante opzione
terapeutica in alternativa, per sottogruppi
selezionati di pazienti, alla mastectomia
radicale dopo IBTR*



I risultati di numerose piccole serie hanno mostrato risultati incoraggianti

- Maulard C, et al. Use of peri-operative or split-course interstitial brachytherapy techniques for salvage irradiation of isolated local recurrences after conservative management of breast cancer. *Am J Clin Oncol* 18:348-52; 1995
- Deutsch M. Repeat high-dose external beam irradiation for in-breast tumor recurrence after previous lumpectomy and whole breast irradiation. *Int J Radiat Oncol Biol Phys* 53:687-91; 2002
- Resch A, et al. Locally recurrent breast cancer: pulse dose rate brachytherapy for repeat irradiation following lumpectomy a second chance to preserve the breast. *Radiology* 225:713-8; 2002
- Hannoun-Levi JM, et al. Partial breast irradiation as second conservative treatment for local breast cancer recurrence. *Int J Radiat Oncol Biol Phys* 60:1385-92; 2004

I risultati di numerose piccole serie hanno mostrato risultati incoraggianti

- Guix B, et al. Exeresis and brachytherapy as salvage treatment for local recurrence after conservative treatment for breast cancer: results of a ten-year pilot study. *Int J Radiat Oncol Biol Phys* 78:804-10; 2010
- Hannoun-Levi JM, et al. Second conservative treatment for ipsilateral breast cancer recurrence using high-dose rate interstitial brachytherapy: preliminary clinical results and evaluation of patient satisfaction. *Brachytherapy* 10:171-7; 2011
- Kauer-Dorner D, et al. Partial breast irradiation for locally recurrent breast cancer within a second breast conserving treatment: alternative to mastectomy? Results from a prospective trial. *Radiother Oncol* 102:96-101; 2012
- Polgár C, et al. Second breast-conserving surgery and reirradiation with interstitial high-dose-rate brachytherapy for the management of

Interstitial Brachytherapy



Second breast-conserving surgery and re-irradiation with interstitial high-dose-rate brachytherapy for the management of intra-breast recurrences. 5-year results

Polgar C et al. Magy Oncol June 2012

- 15 patients
- Prior lumpectomy and postoperative WBI
- Local recurrence \Rightarrow second BCS
- Peri-operative HDR multi-catheter BRT
- Median follow-up of 62 months
- 0/15 local recurrence
- 100% mastectomy-free survival

Second BCS followed by partial breast re-irradiation is a safe and effective option with acceptable cosmetic results and low rate of late side effects

HDR brachytherapy for local recurrences after prior breast radiotherapy: feasibility and preliminary results
Vavassori A et al. WBC 2012

- 12 patients
- Prior quadrantectomy and postoperative WBI
- Local recurrence \Rightarrow second BCS
- HDR multi-catheter BRT 34 Gy/10 fr/BID
- Median follow-up of 6 months
- 0/12 local recurrence
- 100% mastectomy-free survival

Partial breast re-irradiation is a feasible treatment with low complication and good cosmetic results

Accelerated partial breast irradiation with interstitial brachytherapy as second conservative treatment for ipsilateral breast tumour recurrence: Multicentric study of the GEC-ESTRO Breast Cancer Working Group

Hannoun-Levi JM et al. Radiotherapy & Oncology 108, 226–231; 2013

- 217 patients
- Prior lumpectomy and postoperative WBI
- Local recurrence ⇒ second BCS
- Peri-operative HDR multi-catheter BRT
- Median follow-up of 45 months (range 13-123)
- Ten years 2nd LR rate **7.2%** (9/217)
- Ten years DM rate **19.1%**
- Ten years OS rate **76.4%**
- G3 – G4 complication rate **11%**
- Excellent/good cosmetic result **85%**

This study suggests that in case of IBTR, lumpectomy plus MCB is feasible and effective in preventing 2nd LR with an OS rate at least equivalent to those achieved with



**Ipsilateral Breast Tumour Recurrence (IBTR):
Second conservative treatment with Interstitial HDR BRT
Gribaudo S et al. Radiotherapy & Oncology Vol 111 Supp 1
April 2014**

- 22 patients
- Prior lumpectomy and postoperative WBI
- Local recurrence \Rightarrow excision \Rightarrow disease free final margin
- Tumor bed implantation
- 0/22 local recurrence [Median follow up was 68 months (range 174-6)]

A second lumpectomy followed by HDR interstitial brachytherapy is a feasible treatment for IBTR and may be an up to standard alternative to salvage mastectomy, it offers very low complication rate and good cosmesis

Esperienza Torinese

- 1999 – 2014
- 29 pazienti
 - 21 T1
 - 4 Tis
 - 4 T2
- 1° T (27 pz) Stadio I
 - CH + EBRT (60-66 Gy)
- Intervallo medio 10 anni (range 2-25 anni)

■ ISTOLOGIA

- 2 DIN 2
- 3 LI
- 19 DI (5 G₃, 6 G₂, 8 G₁)
- 2 DI + EIC > 25%
- 2 Carcinoma tubulare
- 1 Carcinoma muciparo

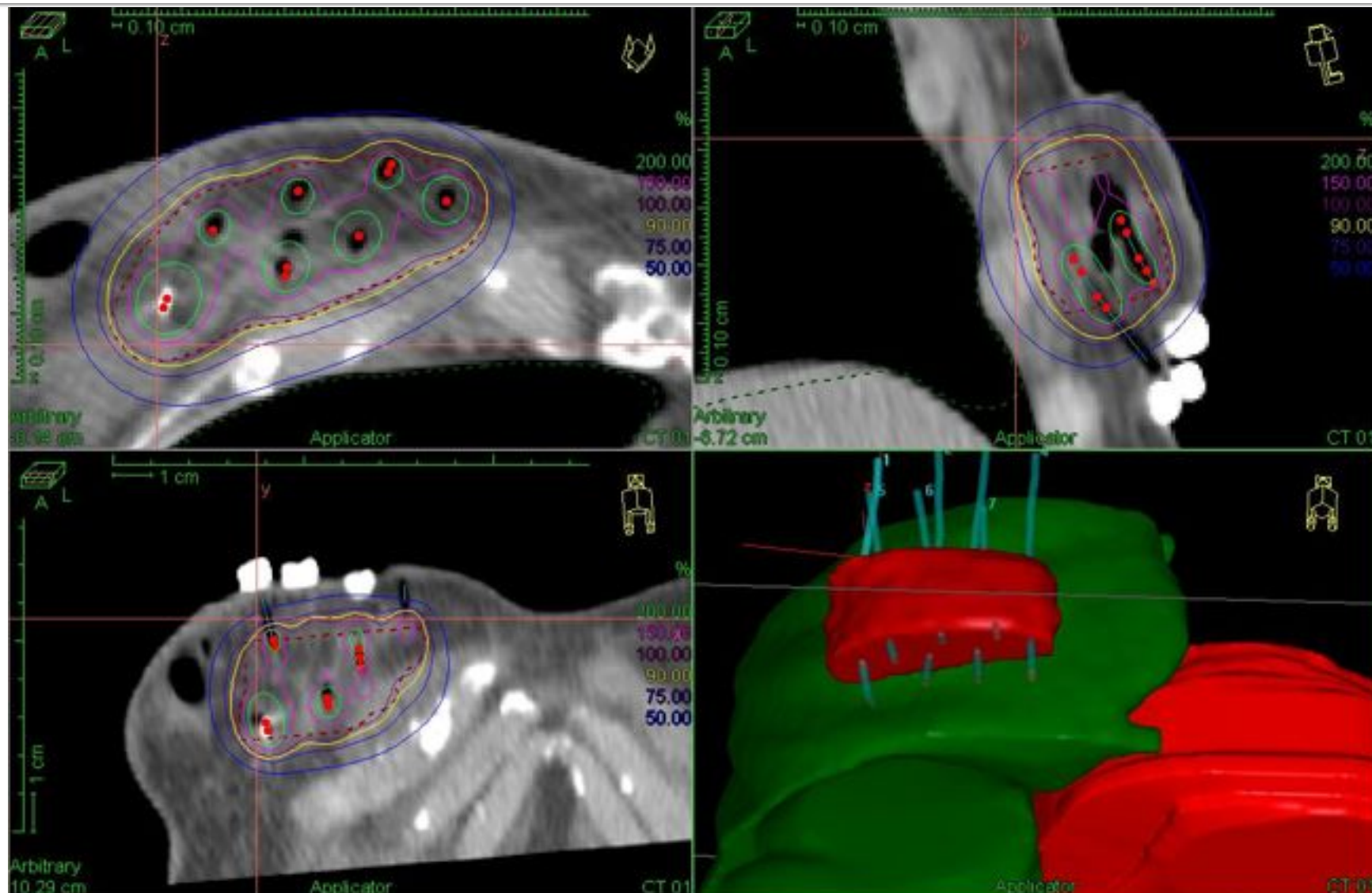
■ LFN, 10 pazienti

Una paziente ha eseguito una irradiazione toracica per un tumore polmonare ed una è stata sottoposta a chirurgia conservativa senza EBRT per un CDIS

Esperienza Torinese

- IBRT
 - \varnothing medio 12 mm (range 5-28 mm)
- Margini indenni (Linee Guida NSABP)
- Infissione nel tempo chirurgico
 - 26 pazienti
- N° medio cateteri 9 (range 5-11)
- Impianto
 - 2 piani
 - 26 pazienti
 - 3 piani
 - 3 pazienti
- Dosi
 - 4000-5000cGy (250 cGy/fr/BID) 14 pazienti (RX e piano di cura in 2D)
 - **3400 cGy (340 cGy/fr/BID) 15 pazienti (TC e piano di cura in 3D)**

Esperienza Torinese



Esperienza Torinese



ROI	Dose [%]	Dose [Gy]	Volume [%]	Volume [ccn]
CTV	100.00	3.4000	90.63	21.40
CTV	66.12	2.2481	100.00	23.70
CTV	150.00	5.1000	39.33	9.32
CTV	200.00	6.8000	17.17	4.07
CTV	90.00	3.0600	96.87	22.96
CTV	100.71	3.4240	90.00	21.33
H	15.12	0.5141	0.01	0.05
H	14.71	0.5000	0.01	0.06
H	29.41	1.0000	-	-
H	44.12	1.5000	-	-
H	4.77	0.1623	10.00	47.96
H	5.03	0.1983	5.00	23.90
rl	44.43	1.5106	0.01	0.10
rl	14.71	0.5000	4.40	44.91
rl	29.41	1.0000	0.52	5.35
rl	44.12	1.5000	0.01	0.11
rl	9.49	0.3226	10.00	101.98
rl	5.74	0.1951	20.00	203.95

Dosimetric characteristics of accelerated partial breast irradiation with CT imaged-based multicatheter interstitial brachytherapy: A single institution's experience

CTV	V90	V100	V150	V200	D90	D100	DHI dose homogeneity index	COIN conformal index	EI external volume index
MEDIA	98	95	44	19	105	77	0,54	0,77	0,2
RANGE	96 - 100	90 - 99	34 - 53	13-29	99 - 109	60 - 92	0,41 - 0,63	0,5 - 0,85	0,1 - 0,35

Coverage (%)

V90	96	93-100
V100	92	90-96
V150	32	23-45
V200	11	5-22
D90	102	99-108
D100	69	53-92

Homogeneity

DHI	0.65	0.50-0.76
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Conformity

COIN	0.68	0.51-0.82
EI	0.32	0.14-0.75

Major T, Polgar C et al. Brachithery 10, 421-426;

SOCIETY BREAST BRACHYTHERAPY TASK GROUP

Keisch M, Arthur D, Patel R, Rivard M, Vicini F – February

Treatment planning dosimetry

- Recommended prescriptive dosimetric parameters that should be met or exceeded:
 - Target coverage: $\geq 90\%$ of the dose delivered to $\geq 90\%$ of the target volume
 - V_{150} : interstitial $< 70 \text{ cm}^3$, balloon catheter $< 50 \text{ cm}^3$
 - V_{200} : interstitial $< 20 \text{ cm}^3$, balloon catheter $< 10 \text{ cm}^3$
 - $\text{DHI} \geq 0.75$ where $\text{DHI} = (1 - V_{150}/V_{100})$
 - Maximum skin isodose: balloon catheter $< 145\%$, typically a limited area
interstitial catheters $\leq 100\%$, typically a larger area



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GEC-ESTRO Recommendations

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)

Csaba Polgár^{a,*}, Erik Van Limbergen^b, Richard Pötter^c, György Kovács^d, Alfredo Polo^e, Jaroslaw Lyczek^f, Guido Hildebrandt^g, Peter Niehoff^h, Jose Luis Guinotⁱ, Ferran Guedea^j, Bengt Johansson^k, Oliver J. Ott^l, Tibor Major^a, Vratislav Strnad^l, On behalf of the GEC-ESTRO breast cancer working group

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Dosimetric characteristics of accelerated partial breast irradiation with CT imaged-based multicatheter interstitial brachytherapy: A single institution's experience

OAR HEART	Dmax %	V5 Cc	V10 cc	D5 %	D10 %
MEDIA	21	10	0,03	10	9
RANGE	13 – 32	0 – 54	0 – 21	4,6 – 18	3,6 – 15,5

OAR SKIN	Dmax %	DA ARTICOLO
MEDIA	57	55
RANGE	31 – 72	12 - 75

Heart (left-sided lesions, $n = 20$)

D_{max} (%)	21	4–40
V_{5Gy} (cm ³)	12.8	0–83.0
V_{10Gy} (cm ³)	0.3	0–4.2
V_{heart} ($n = 9$) (cm ³)	471.4	233.6–849.0
V5 (%)	47	19–81
V15 (%)	4	0–14
D5 (%)	13	9–22
D10 (%)	11	7–17

Major T, Polgar C et al. Brachithery 10, 421-426;

Dosimetric characteristics of accelerated partial breast irradiation with CT imaged-based multicatheter interstitial brachytherapy: A single institution's experience

OAR Ipsilateral Lung	Dmax %	V5 cc	V10 cc	V15 cc	D10 %	D20 %
MEDIA	43	69	12	2	13	8
RANGE	20 – 66	5 – 161	0 – 47	0 – 8	7 – 20	3 – 13

Ipsilateral lung

D_{\max} (%)	44	7–75
$V_{5\text{Gy}}$ (cm ³)	50.6	0–160.6
$V_{10\text{Gy}}$ (cm ³)	6.7	0–39.5
$V_{15\text{Gy}}$ (cm ³)	0.4	0–7.9
$V_{\text{lung}} (n = 26)$ (cm ³)	1035.4	332.3–1683.0
V10 (%)	17	0–33
V30 (%)	1	0–4
D10 (%)	13	6–22
D20 (%)	9	4–15

Major T, Polgar C et al. Brachithery 10, 421-426;

Esperienza Torinese

- Complicanze peri-operatorie
 - Una infezione della ferita chirurgica 1 mese dopo l'impianto
- Complicanze tardive
 - Un sieroma con risoluzione spontanea dopo 18 mesi

Terapia Adiuvante

- **CT** [EC_(1:21) x 4 cicli ± Taxolo_(1:8) x 12 cicli]
 - 4 pazienti
- **OT**
 - **Tamoxifen** 7 pazienti
 - **IA** 16 pazienti

Esperienza Torinese

- Follow up mediano 41 mesi (range 174-3)
 - 27 pazienti
 - 1 paziente persa al follow up dopo un anno
 - 1 paziente ha terminato da meno di un mese
- **CL 100%**
- **DFS 100%**

Esiti Cosmetici (Scala del NSABP)

- 14 pazienti soddisfacente
- 14 pazienti eccellente

Common Terminology Criteria for Adverse Events v3.0 (CTCAE)

- 5 pazienti fibrosi o teleangectasie di grado 2
- 23 pazienti buoni o ottimi esiti cosmetici

APBI – MCB – HDR

Ulteriori campi di applicazione



PB BRT for breast cancer after MANTLE RT

Chada et al. Am J Clin Oncol, 2009

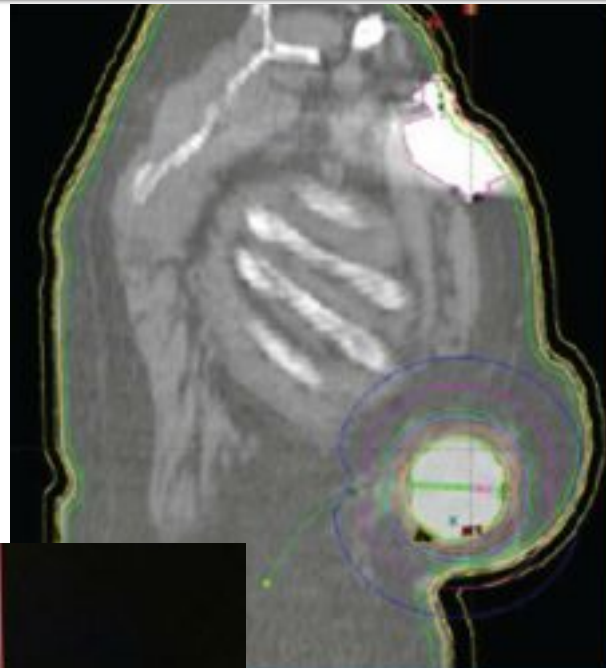
- 5 patients
- Prior RT for Hodgkin's Disease (median dose 40 Gy)
- Multicatheter technique
- Good cosmetics
- No relapse

Conclusion

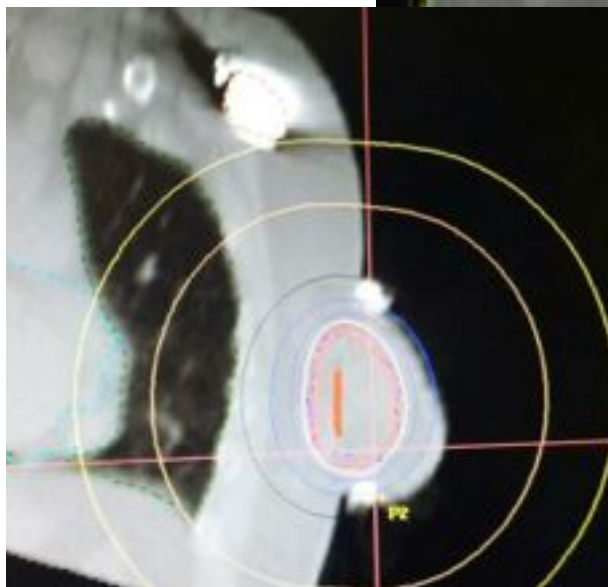
- ***Low complication rate***
- ***Acceptable cosmetic results***
- ***PB-BRT as an alternative to mastectomy***

Avoiding Mastectomy: Accelerated Partial Breast Irradiation for Breast Cancer Patients with Pacemakers or Defibrillators

Randal Croshaw R Ann Surg Oncol 2011



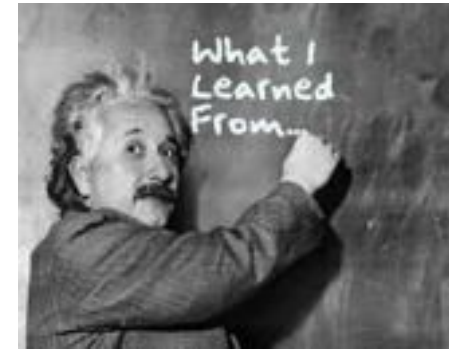
- APBI-BT in patients with pacemakers or AICD_s who desire breast preservation seems to be a technically safe and reasonable application of targeted radiation therapy



**MCB eseguito presso il nostro
Centro: Dose totale 1 Gy
Dose limite accettata in letteratura: 2
Gy**



**Take
home message*



- ***È possibile una seconda chirurgia conservativa seguita da MCB – HDR, per le IBTR insorte dopo chirurgia conservativa & EBRT ?***
- È fattibile! Può essere una valida soluzione, alternativa allo standard della mastectomia
- Basso tasso di complicanze ed una buona cosmesi
- Possono essere necessari, per validare il ruolo della metodica, un follow-up più lungo ed una casistica più numerosa

Riteniamo che utilizzando rigidi criteri di selezione, ci sia la possibilità di personalizzare le scelte terapeutiche e di offrire alle donne una seconda opportunità di

1-12-85

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