NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)®

Breast Cancer

Version 2.2013

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NCCN Guidelines Version 2.2013
Breast Cancer

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Overview

The Breast Cancer Clinical Practice Guidelines presented here are the work of the members of the NCCN Breast Cancer Clinical Practice Guidelines Panel. Categories of evidence were assessed and are noted on the algorithms and in the text. Although not explicitly stated at every decision point of the guidelines, patient participation in prospective clinical trials is the preferred option of treatment for all stages of breast cancer.

The American Cancer Society estimates that 234,580 Americans will be diagnosed with breast cancer and 40,030 will die of the disease in the United States in 2013.[1] Breast cancer is the most common malignancy in women in the United States and is second only to lung cancer as a cause of cancer death.

The incidence of breast cancer has increased steadily in the United States over the past few decades, but breast cancer mortality appears to be declining,[2,3] suggesting a benefit from early detection and more effective treatment.

The etiology of the vast majority of breast cancer cases is unknown. However, numerous risk factors for the disease have been established. These risk factors include: female gender; increasing patient age; family history of breast cancer at a young age; early menarche; late menopause; older age at first live childbirth; prolonged hormone replacement therapy; previous exposure to therapeutic chest wall irradiation; benign proliferative breast disease; increased mammographic breast density; and genetic mutations such as of the *BRCA1/2* genes. However, except for female gender and increasing patient age, these risk factors are associated with only a minority of breast cancers. Women with a strong family history of breast cancer should be evaluated according to the NCCN Guidelines for Genetic/Familial High-Risk Assessment. Women at increased risk for breast cancer (generally those with ≥1.67% 5-year risk for breast cancer using the Gail model of risk assessment[4]) may consider risk reduction strategies (see NCCN Guidelines for Breast Cancer Risk Reduction).

Proliferative abnormalities of the breast are limited to the lobular and ductal epithelium. In both the lobular and ductal epithelium, a spectrum of proliferative abnormalities may be seen, including hyperplasia, atypical hyperplasia, in situ carcinoma, and invasive carcinoma.[5] Approximately 85% to 90% of invasive carcinomas are ductal in origin.[6] The invasive ductal carcinomas include unusual variants of breast cancer, such as mucinous, adenoid cystic, and tubular carcinomas, which have especially favorable natural histories.

Staging

All patients with breast cancer should be assigned a clinical stage of disease, and, if appropriate evaluation is available, a pathologic stage of disease. The routine use of staging allows for efficient identification of local treatment options, assists in identifying systemic treatment options, allows for the comparison of outcome results across institutions and clinical trials, and provides baseline prognostic information. Effective January 2010, the AJCC implemented a revision of the Cancer Staging Manual (seventh edition) containing important changes and additions to the TNM staging system for breast cancer.[7] This revision differs from the 2003 edition of the AJCC staging manual by providing more direction relating to the specific methods of clinical and pathologic tumor measurement; recommending that all invasive cancers should be assigned a combined histologic tumor grade using the Elston-Ellis modification of the Scarff-Bloom-Richardson grading system; providing clarification of the classification of isolated tumor cells in axillary lymph node (ALN) staging; subdividing stage I into stage IA and IB based

Fattori di rischio

Età

Storia familiare

Precedente storia personale

Aumentata esposizione agli estrogeni

Nulliparità

Prima gravidanza dopo i 30 anni

Dieta e stile di vita

Esposizione a radiazioni prima dei 40 anni

Fattori di rischio

Predisposizione genetica < 10%

Ereditata sotto forma di carattere autosomico dominante con penetranza limitata

Può essere trasmessa a entrambi i sessi.

I trasmettitori del gene anomalo non necessariamente si ammalano

Geni BRCA1 e BRCA2, situati rispettivamente sul braccio lungo dei cromosomi 17 e 13

ASPETTI DIAGNOSTICI

Segni e sintomi alla presentazione:

- Tumefazione palpabile
- Tumefazione e dolore ascellare
- Ispessimento
- Dolore
- Secrezione dal capezzolo
- Retrazione del capezzolo
- Edema o eritema cutaneo
- Noduli cutanei

Diagnosi

Ispezione

Palpazione

Valutazione linfonodi regionali

Mammografia

Ecografia

RM

Screening Mammografico

Obiettivi

Diagnosi precoce in donne asintomatiche

Riduzione della mortalità conseguente alla diagnosi precoce

Riduce la mortalità del 26% in donne di età compresa 50 e 70 anni

American Cancer Society

1° screeening mammografico dall'età di 40 anni
Mammografia ogni 1-2 anni tra i 40 e 49 anni

Mammografia annuale successivamente

In Europa

Mammografia ogni 2 anni tra i 50 e 69 anni

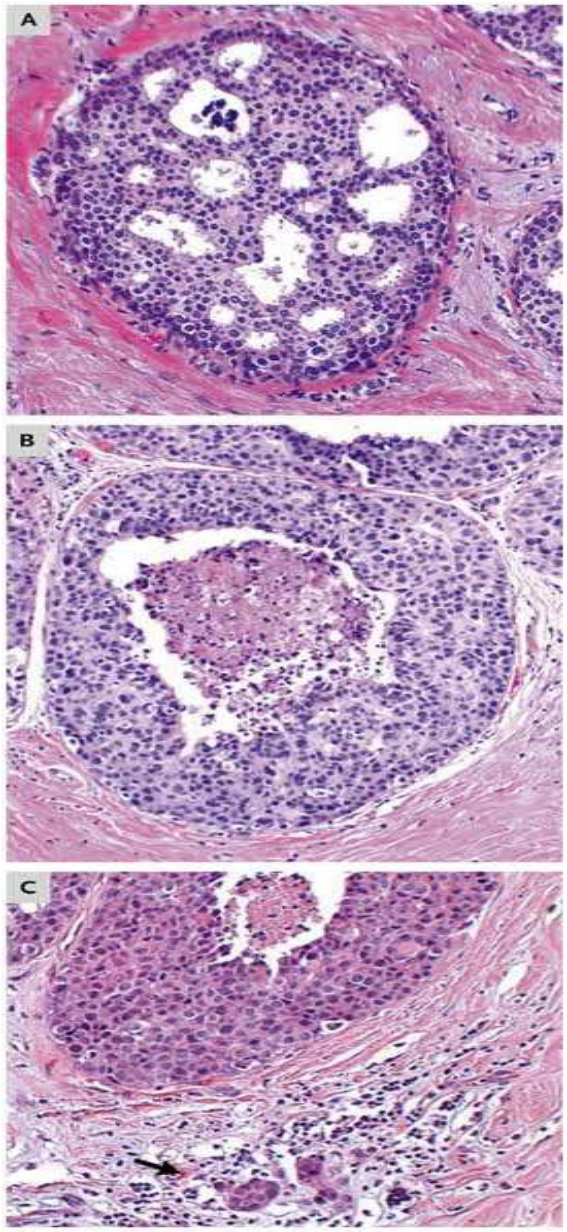
CARCINOMA DUTTALE IN SITU

Proliferazione di cellule epiteliali maligne sviluppata all'interno dei dotti.

Assenza di invasione della membrana basale.

Assenza di rischio di metastasi sia linfonodali che a distanza.

Rappresenta la prima tappa della cancerizzazione mammaria, compresa tra l'iperplasia atipica e le forme infiltranti.



Precursore non obbligato di forme infiltranti

INCIDENZA

Era pre-mammografica

3-5 % di tutti i tumori mammari

Si trattava quasi sempre di lesioni palpabili, a volte molto estese, o di forme associate a una malattia di Paget o ad una secrezione ematica

Programmi di screening mammografico

incidenza 20-30%

oltre il 90% dei casi sono clinicamente occulti

... e, in effetti, il riscontro dei DCIS sta aumentando con la diffusione della mammografia.

PERCENTUALE DI RISCONTRO DI CARCINOMI IN SITU

	%
PRE - MAMMOGRAFIA	1 - 5
MAMMOGRAFIA < 1980	8
MAMMOGRAFIA > 1980	25 - 30
MAMMOGRAFIA 2000	40 - 50

Di Maggio, Seminario Pezcoller, Trento 2006

Screening in donne alto rischio

Annuale iniziando 5 anni prima dell'età che al momento della diagnosi aveva la parente più giovane affetta da cr mammario:

- alto rischio familiare
- BRCA 1 -2 positivo

Diagnosi per lesioni palpabili o evidenziabili all’ Rx mammografia

Histologic Classification and Incidence of Invasive Breast Cancer

HISTOLOGIC TYPE	INCIDENCE (%)
Invasive ductal carcinoma	85
Invasive lobular carcinoma	4–10
Mucinous carcinoma	
Medullary carcinoma	
Papillary carcinoma	3–6
Tubular carcinoma	
Adenoid cystic carcinoma	
Secretory (juvenile) carcinoma	
Apocrine carcinoma	
Carcinoma with metaplasia	

Adapted from Azzopardi JG, Chepick OF, Hartman WH, et al: The World Health Organization histological typing of breast tumors, 2nd ed. Am J Clin Pathol 1982;78:806.

Table 1

American Joint Committee on Cancer (AJCC)
TNM Staging System For Breast Cancer

Primary Tumor (T) The T classification of the primary tumor is the same regardless of whether it is based on clinical or pathologic criteria, or both. Size should be measured to the nearest millimeter. If the tumor size is slightly less than or greater than a cutoff for a given T classification, it is recommended that the size be rounded to the millimeter reading that is closest to the cutoff. For example, a reported size of 1.1 mm is reported as 1 mm, or a size of 2.01 cm is reported as 2.0 cm. Designation should be made with the subscript "c" or "p" modifier to indicate whether the T classification was determined by clinical (physical examination or radiologic) or pathologic measurements, respectively. In general, pathologic determination should take precedence over clinical determination of T size.

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted
T1	Tumor ≤20 mm or less in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules).
Note: Invasion of the dermis alone does not qualify as T4	
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma

Table 1 (continued)

Regional Lymph Nodes (N)

Clinical

NX		Regional lymph nodes cannot be assessed (e.g., previously removed)
N0		No regional lymph node metastasis
N1		Metastases to movable ipsilateral level I, II axillary lymph node(s)
N2		Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary nodes in the *absence* of clinically evident axillary lymph node metastases
	N2a	Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
	N2b	Metastases only in clinically detected* ipsilateral internal mammary nodes and in the *absence* of clinically evident level I, II axillary lymph node metastases
N3		Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
	N3a	Metastasis in ipsilateral infraclavicular lymph node(s)
	N3b	Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
	N3c	Metastasis in ipsilateral supraclavicular lymph node(s)

**Note* : *Clinically detected* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration.

Pathologic (pN)*

pNX	Regional lymph nodes cannot be assessed (e.g., previously removed, or not removed for pathologic study)
pN0	No regional lymph node metastasis histologically

Note : Isolated tumor cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm, or single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

pN0(i-)	No regional lymph node metastasis histologically, negative IHC
pN0(I+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
pN0(mol-)	No regional lymph node metastases histologically, negative molecular findings (RT-PCR)
pN0(mol+)	Positive molecular findings (RT-PCR),** but no regional lymph node metastases detected by histology or IHC

* Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for "sentinel node," for example, pN0(sn).

** RT-PCR: reverse transcriptase/polymerase chain reaction.

Table 1 (continued)

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage 0	Tis	N0	M0	**Stage IIIA**	T0	N2	M0
Stage IA	T1*	N0	M0		T1*	N2	M0
Stage IB	T0	N1mi	M0		T2	N2	M0
	T1*	N1mi	M0		T3	N1	M0
Stage IIA	T0	N1**	M0		T3	N2	M0
	T1*	N1**	M0	**Stage IIIB**	T4	N0	M0
	T2	N0	M0		T4	N1	M0
Stage IIB	T2	N1	M0		T4	N2	M0
	T3	N0	M0	**Stage IIIC**	Any T	N3	M0
				Stage IV	Any T	Any N	M1

* T1 includes T1mi

** T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

- M0 includes M0(i+).
- The designation pM0 is not valid; any M0 should be clinical.
- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.
- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.
- Postneoadjuvant therapy is designated with "yc" or "yp" prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

HISTOLOGIC GRADE (G)

All invasive breast carcinomas should be graded. The Nottingham combined histologic grade (Elston-Ellis modification of Scarff–Bloom–Richardson grading system) is recommended.[1,2] The grade for a tumor is determined by assessing morphologic features (tubule formation, nuclear pleomorphism, and mitotic count), assigning a value of 1 (favorable) to 3 (unfavorable) for each feature, and adding together the scores for all three categories. A combined score of 3–5 points is designated as grade 1; a combined score of 6–7 points

HISTOLOGIC GRADE (NOTTINGHAM COMBINED HISTOLOGIC GRADE IS RECOMMENDED)

GX	Grade cannot be assessed
G1	Low combined histologic grade (favorable)
G2	Intermediate combined histologic grade (moderately favorable)
G3	High combined histologic grade (unfavorable)

HISTOPATHOLOGIC TYPE

The histopathologic types are the following:

In situ Carcinomas

NOS (not otherwise specified)
Intraductal
Paget's disease and intraductal

Invasive Carcinomas

NOS
Ductal
Inflammatory
Medullary, NOS
Medullary with lymphoid stroma
Mucinous
Papillary (predominantly micropapillary pattern)
Tubular
Lobular
Paget's disease and infiltrating
Undifferentiated
Squamous cell
Adenoid cystic
Secretory
Cribriform

[1]Harris L, Fritsche H, Mennel R, et al. American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. J Clin Oncol 2007;25:5287–312.

[2]Singletary SE, Allred C, Ashley P, et al. Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol 2002;20:3628–36.

Stadiazione

Diagnosi

Terapia

Stadiazione

Rx torace

Ecografia epatica

Scintigrafia ossea

per valutare l’estensione di malattia

decidere l’approccio terapeutico

CHIRURGIA: mastectomia
conservativa
linfectomia ascellare, biopsia LN sentinella

TERAPIA SISTEMICA: chemioterapia
ormonoterapia
farmaci a bersaglio molecolare

RADIOTERAPIA

Ipotesi	
Hellman, JCO1994	**Il carcinoma della mammella è una malattia eterogenea, che può essere sistemica già al momento della diagnosi, ma anche rimanere localizzata.** **Le metastasi insorgono in funzione della crescita e della progressione tumorale** **Per aumentare la possibilità di cura è necessario controllare loco-regionalmente la malattia.** **È ipotizzabile che il controllo loco-regionale possa incidere sulla sopravvivenza globale attraverso una riduzione del processo di metastatizzazione**

Ipotesi	Assunto	Il trattamento loco-regionale può prevenire la diffusione a distanza della malattia e quindi influenzare la sopravvivenza?
Halsted, 1895	Il cr mammario diffonde dalla sede iniziale ai linfonodi loco-regionali e solo più tardivamente metastatizza a distanza	**Si**
Fisher, 1980	Il cr mammario è una malattia micrometastatica già al momento della diagnosi	**No**

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Invasive Breast Cancer

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LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0

Lumpectomy with surgical axillary staging (category 1)[j,k,l]

- **≥4 positive[o] axillary nodes** → **Radiation therapy to whole breast with or without boost[p] (by photons, brachytherapy, or electron beam) to tumor bed (category 1), infraclavicular region and supraclavicular area. Strongly consider radiation therapy to internal mammary nodes[q] (category 2B). Radiation therapy should follow chemotherapy when chemotherapy is indicated.**
- **1-3 positive axillary nodes** → **Radiation therapy to whole breast with or without boost[p] (by photons, brachytherapy, or electron beam) to tumor bed (category 1) following chemotherapy when chemotherapy is indicated. Strongly consider radiation therapy to infraclavicular region and supraclavicular area (category 2B). Strongly consider radiation therapy to internal mammary nodes[q] (category 2B). Radiation therapy should follow chemotherapy when chemotherapy is indicated.**

or

- **Negative axillary nodes** → **Radiation therapy to whole breast with or without boost[p] (by photons, brachytherapy, or electron beam) to tumor bed or consideration of partial breast irradiation (PBI) in selected patients.[p,r] Radiation therapy should follow chemotherapy when chemotherapy is indicated.[s]**

→ See BINV-4

Total mastectomy with surgical axillary staging[j,k,m] (category 1) ± reconstruction[n] → See Locoregional Treatment (BINV-3)

or

If T2 or T3 and fulfills criteria for breast-conserving therapy except for size[l] → Consider Preoperative Chemotherapy Guideline (BINV-10)

[j] See Surgical Axillary Staging (BINV-D).

[k] See Axillary Lymph Node Staging (BINV-E) and Margin Status in Infiltrating Carcinoma (BINV-F).

[l] See Special Considerations to Breast-Conserving Therapy (BINV-G).

[m] Except as outlined in the NCCN Guidelines for Genetics/Familial High-Risk Assessment: Breast and Ovarian and the NCCN Guidelines for Breast Cancer Risk Reduction, prophylactic mastectomy of a breast contralateral to a known unilateral breast cancer is discouraged. When considered, the small benefits from contralateral prophylactic mastectomy for women with unilateral breast cancer must be balanced with the risk of recurrent disease from the known ipsilateral breast cancer, psychological and social issues of bilateral mastectomy, and the risks of contralateral mastectomy. The use of a prophylactic mastectomy contralateral to a breast treated with breast-conserving therapy is very strongly discouraged.

[n] See Principles of Breast Reconstruction Following Surgery (BINV-H).

[o] Consider imaging for systemic staging, including diagnostic CT or MRI, bone scan, and optional FDG PET/CT (category 2B) (See BINV-1).

[p] See Principles of Radiation Therapy (BINV-I).

[q] Radiation therapy should be given to the internal mammary lymph nodes if they are clinically or pathologically positive, otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where radiation therapy is delivered to the internal mammary lymph nodes.

[r] PBI may be administered prior to chemotherapy.

[s] Breast irradiation may be omitted in those 70 y of age or older with estrogen-receptor positive, clinically node-negative, T1 tumors who receive adjuvant endocrine therapy (category 1).

RT POST BCS

Trattamento Standard

Volume bersaglio

intera ghiandola mammaria

±

stazioni di drenaggio linfonodale

Riduce significativamente il rischio di recidiva loco-regionale

RT POST BCS

GLI STUDI RANDOMIZZATI

STUDIO	N° Pz	RL RT-	RL RT+	OS RT-	OS RT+	Follow-up mediano (anni)
Clark JNCI 1996	**837**	**35%**	**11%** p< 0.001	**76%**	**79%** p = 0.33	**7.6**
Forest Lancet 1996	585	**24.5%**	**6.9%**	**83%°**	**83%°**	**5.7**
Liljegren JCO 1999	381	**24%**	**8.5%** p = 0.0001	**78%***	**77.5%*** p = 0.99	**9**

° a 5, * a 10 anni

STUDIO	N° Pz	RL RT-	RL RT+	OS RT-	OS RT+	Follow-up mediano (anni)
Veronesi Ann Oncol 2001	579	23.5%**	5.8%**	76.9%**	82.4%** p = 0.326	9
Holli JCO 2009	264	27.2%	11.6% p = 0.0013	98.6%*	97.1%* p = 0.72	12.1
Malmström EJC 2003	1178	14%*	4%* p < 0.001	93%*	94%* p = 0.41	5
Fisher NEJM 2002	1137	39.2%°	14.3%° p < 0.001	46%°	47%° p = 0.57	12

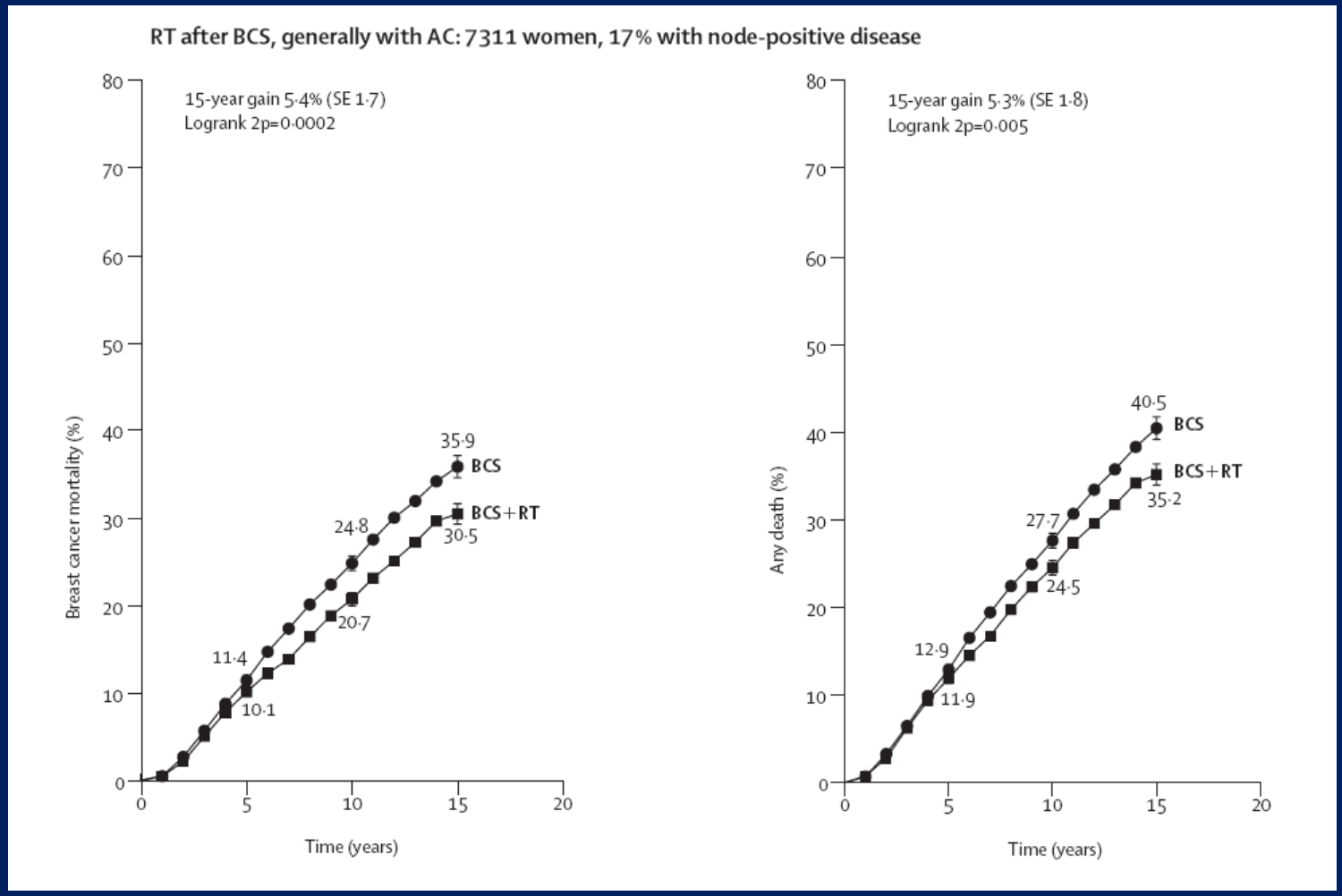
* a 5 anni, ** a 10 anni, ° a 20 anni

La discrepanza tra entità della riduzione di recidiva e mancato vantaggio in OS potrebbe dipendere da

inadeguata potenza statistica dei singoli studi

follow-up non sufficientemente lungo

EBCTCG META-ANALYSIS : RESULTS



EBCTCG:Lancet 2005

EBCTCG META-ANALYSIS : RESULTS

Ipotizzando l'assenza di altre cause di morte, 1 morte per tumore della mammella potrebbe essere risparmiata nei 15 anni successivi alla radioterapia per ogni 4 recidive prevenute

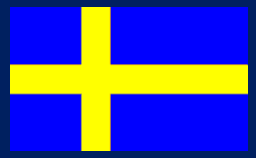
EBCTCG:Lancet 2005

CDIS: STUDI RANDOMIZZATI

NSABP B-17 — 1985-1990

EORTC 10583 — 1986-1996

UK – ANZ — 1990-1998



SWEDISH — 1987-1999

MASTECTOMIA: INDICAZIONI

- Malattia multicentrica
- Lesioni ≥ 4-5 cm
- Margini inadeguati dopo chirurgia conservativa
- Controindicazioni a RT
- Cause d'insuccesso:
  - Persistenza di residuo ghiandolare
  - Non riconoscimento di focolai invasivi

MASTECTOMIA PER MALATTIA NON INVASIVA

DOPO LA MASTECTOMIA, SEGUITA O MENO DALLA RICOSTRUZIONE, **NON** VI È INDICAZIONE ALLA RT COMPLEMENTARE ???

RADIOTERAPIA DOPO CHIRURGIA CONSERVATIVA

- Volume irradiato

  Mammella

  Limitare l'irradiazione cardiaca e polmonare

- Dose

  Singola 1.8-2 Gy

  Totale 50.4-50 Gy

- Boost

  su letto tumorale (10-20 Gy)

Trial EORTC 22881-10882
Recicive locali in funzione dell'età: boost vs non boost

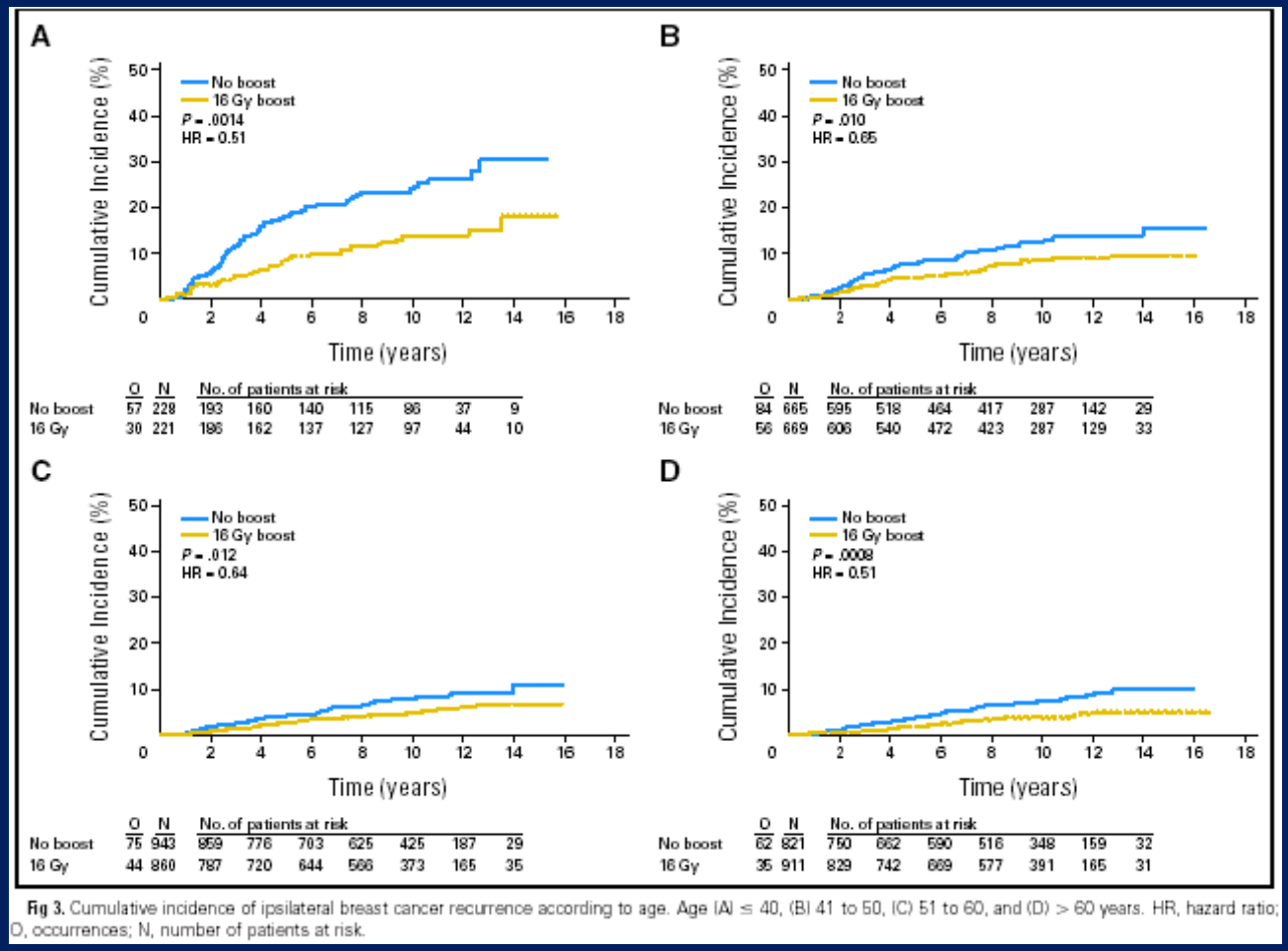


Fig 3. Cumulative incidence of ipsilateral breast cancer recurrence according to age. Age (A) ≤ 40, (B) 41 to 50, (C) 51 to 60, and (D) > 60 years. HR, hazard ratio; O, occurrences; N, number of patients at risk.

Le mastectomie di salvataggio si riducono del 41% !!

Bartelink et al. J Clin Oncol , 2007

- Tecnica di irradiazione

  2 campi tangenziali, generalmente contrapposti

  Fotoni di 4-6 MV

- Boost

  Fotoni, elettroni, brachiterapia, IORT

SCHEMI IPOFRAZIONATI

STUDI RANDOMIZZATI: CONFRONTO BED

Studio	Schema RT			α/β 4 Gy	α/β 2Gy	α/β 2.5 Gy	α/β 3Gy	α/β 10 Gy
Standard	2 Gy	→	50 Gy	75	100	90	83.33	60
Standard + Boost	2 Gy	→	60 Gy	90	120	108	100	72
RMH/GOC *Lancet Oncol 2006*	3.3 Gy	→	42.9 Gy	78.29	113.68	99.53	90.03	57.06
START A *Lancet Oncol 2008*	3.2 Gy	→	41.6 Gy	74.88	108.16	94.85	85.97	54.91
RMH/GOC START A	3 Gy	→	39 Gy	68.23	97.50	85.80	78.00	50.70
START B *Lancet 2008*	2.67 Gy	→	40 Gy	66.78	93.52	82.82	75.69	50.74
Whelan et al *JNCI 2002* *NEJM 2010*	2.66 Gy	→	42.5 Gy	70.86	99.16	87.84	80.30	53.88

STUDI RANDOMIZZATI: CONFRONTO EQD2

Studio	Schema RT			α/β 4 Gy*	α/β 2Gy	α/β 2.5 Gy	α/β 3Gy	α/β 10 Gy
Standard	2 Gy	→	50 Gy	50	50	50	50	50
Standard + Boost	2 Gy	→	60 Gy	60	60	60	60	60
RMH/GOC *Lancet Oncol 2006*	3.3 Gy	→	42.9 Gy	52.19	56.84	55.29	54.05	47.55
START A *Lancet Oncol 2008*	3.2 Gy	→	41.6 Gy	49.92	54.08	52.69	51.58	45.76
RMH/GOC START A	3 Gy	→	39 Gy	45.50	48.75	47.67	46.80	42.25
START B *Lancet 2008*	2.67 Gy	→	40 Gy	44.52	46.76	46.01	45.42	42.3
Whelan et al *JNCI 2002* *NEJM 2010*	2.66 Gy	→	42.5 Gy	47.24	49.58	48.80	48.18	44.90

NCCN® Practice Guidelines in Oncology – v.1.2010

Invasive Breast Cancer

Whole Breast Radiation:

Target delineation includes the majority of the breast tissue, and is best done by both clinical assessment and CT-based treatment planning. A uniform dose distribution is the objective, using compensators such as wedges, forward planning using segments, or intensity modulated radiation therapy (IMRT). The breast should receive a dose of 45-50 Gy in 1.8 - 2 Gy per fraction, or 42.5 Gy at 2.66 Gy per fraction. A boost to the tumor bed is recommended in patients at higher risk for local failure, (age < 50, positive axillary nodes, lymphovascular invasion, or close margins). This can be achieved with brachytherapy or electron beam or photon fields. Typical doses are 10-16 Gy at 2 Gy/fx. All dose schedules are given 5 days per week.

should also feel confident with the 15-fraction regimen. Assuming an α/β value of 3.0 Gy for late adverse effects in the breast, 40 Gy in 15 fractions of 2.67 Gy is equivalent to 45.5 Gy in 2.0 Gy fractions, or to 47 Gy in 2.0 Gy fractions assuming a/b = 2.0 Gy for brachial plexus.[1] This 15-fraction schedule delivered over 3 weeks is now recommended by the National Institute for Clinical Excellence as standard of care for adjuvant radiotherapy for breast cancer patients in the United Kingdom (UK).[2]

The Breast 19 (2010) 159–162

Contents lists available at ScienceDirect

The Breast

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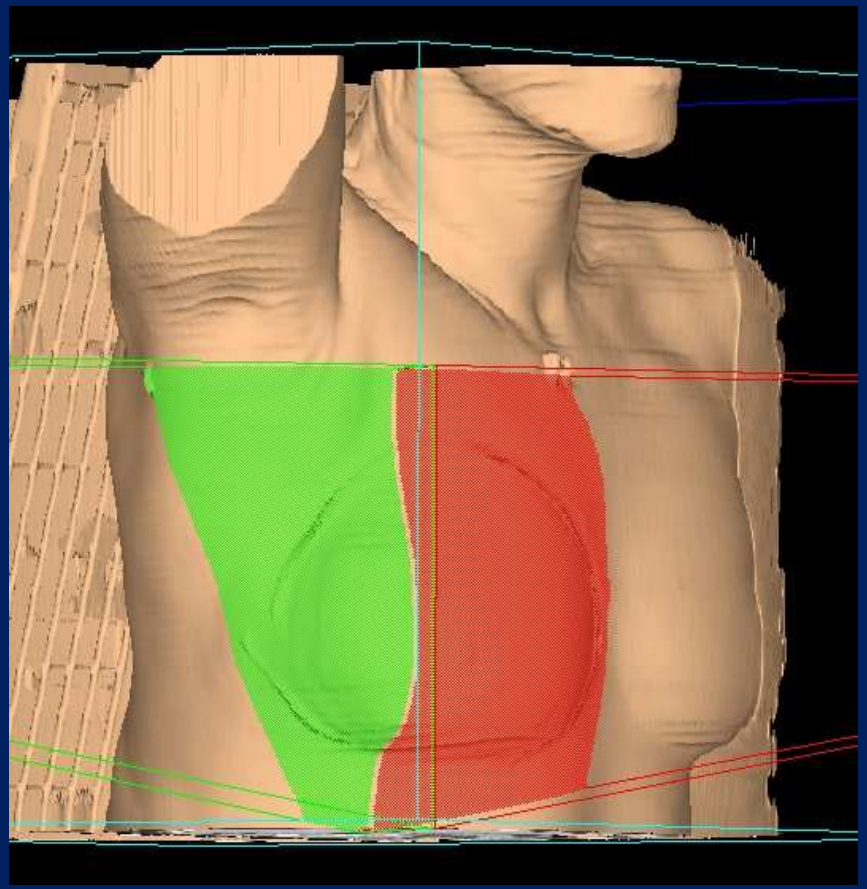
Original article

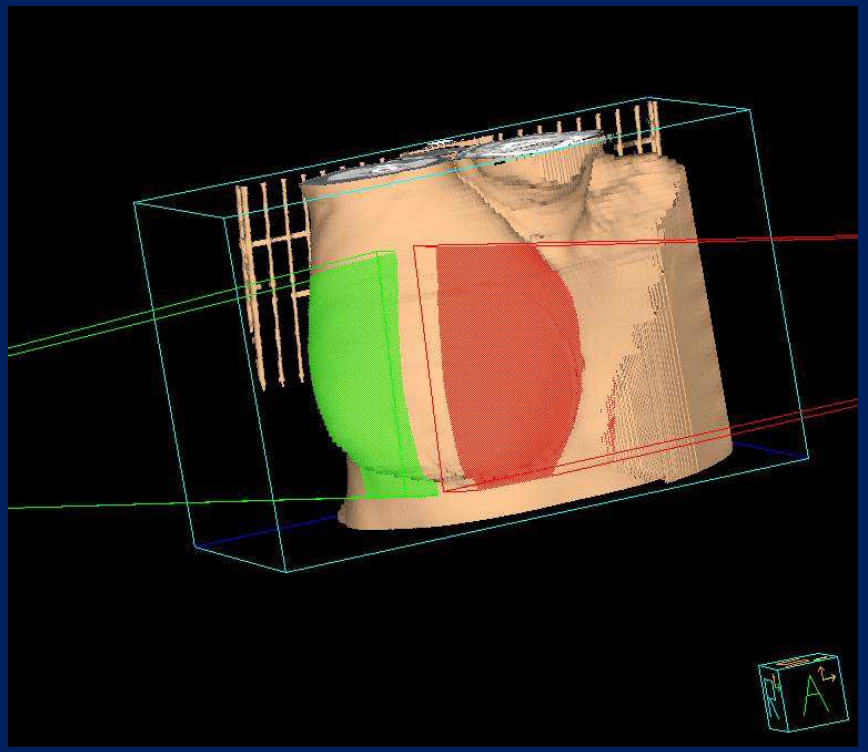
Fewer fractions of adjuvant external beam radiotherapy for early breast cancer are safe and effective and can now be the standard of care

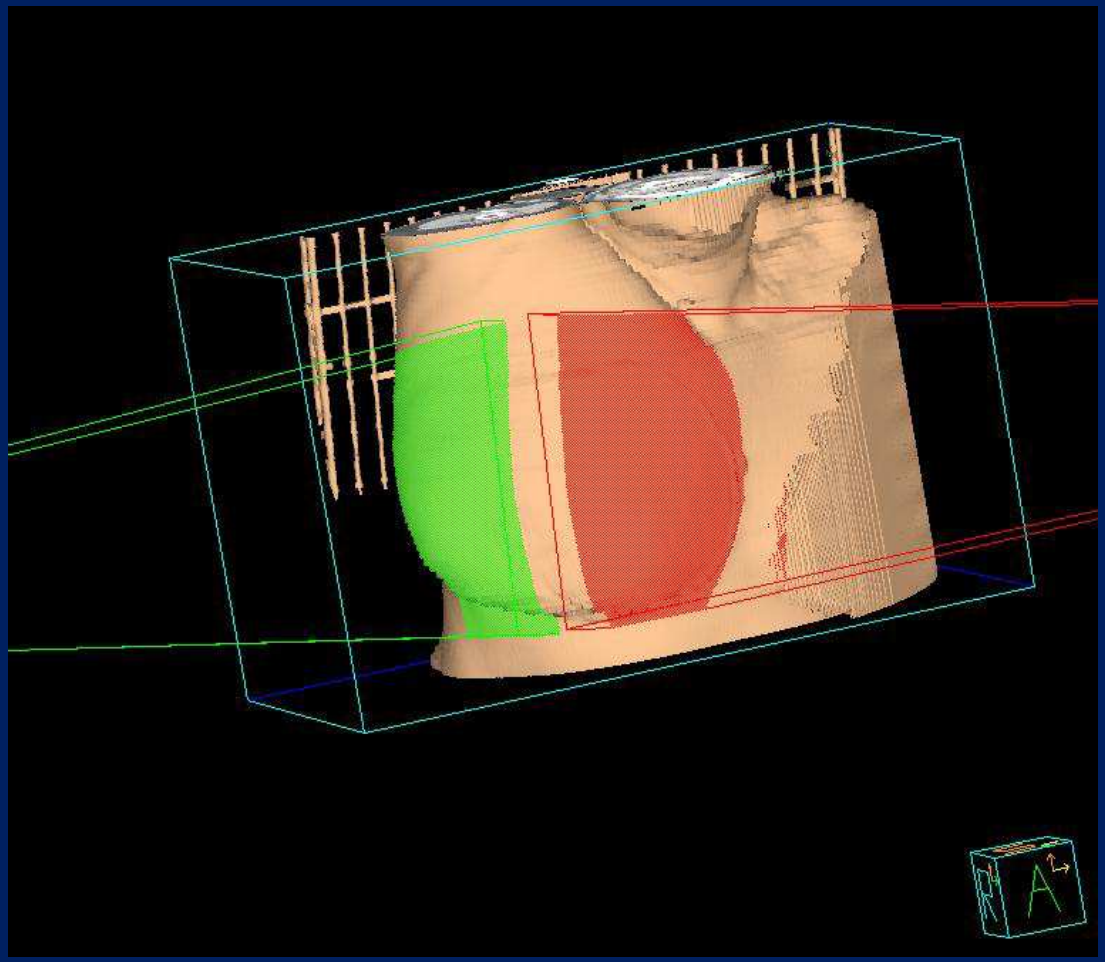
Why the UK's NICE accepts fewer fractions as the standard of care for adjuvant radiotherapy in early breast cancer

Adrian Harnett*

Norfolk & Norwich University Hospital, Colney Lane, Norwich NR4 7UY, UK








6 MV
Pct POI, "RIF" = 50.0264 Gy
112.0 %
108.0 %
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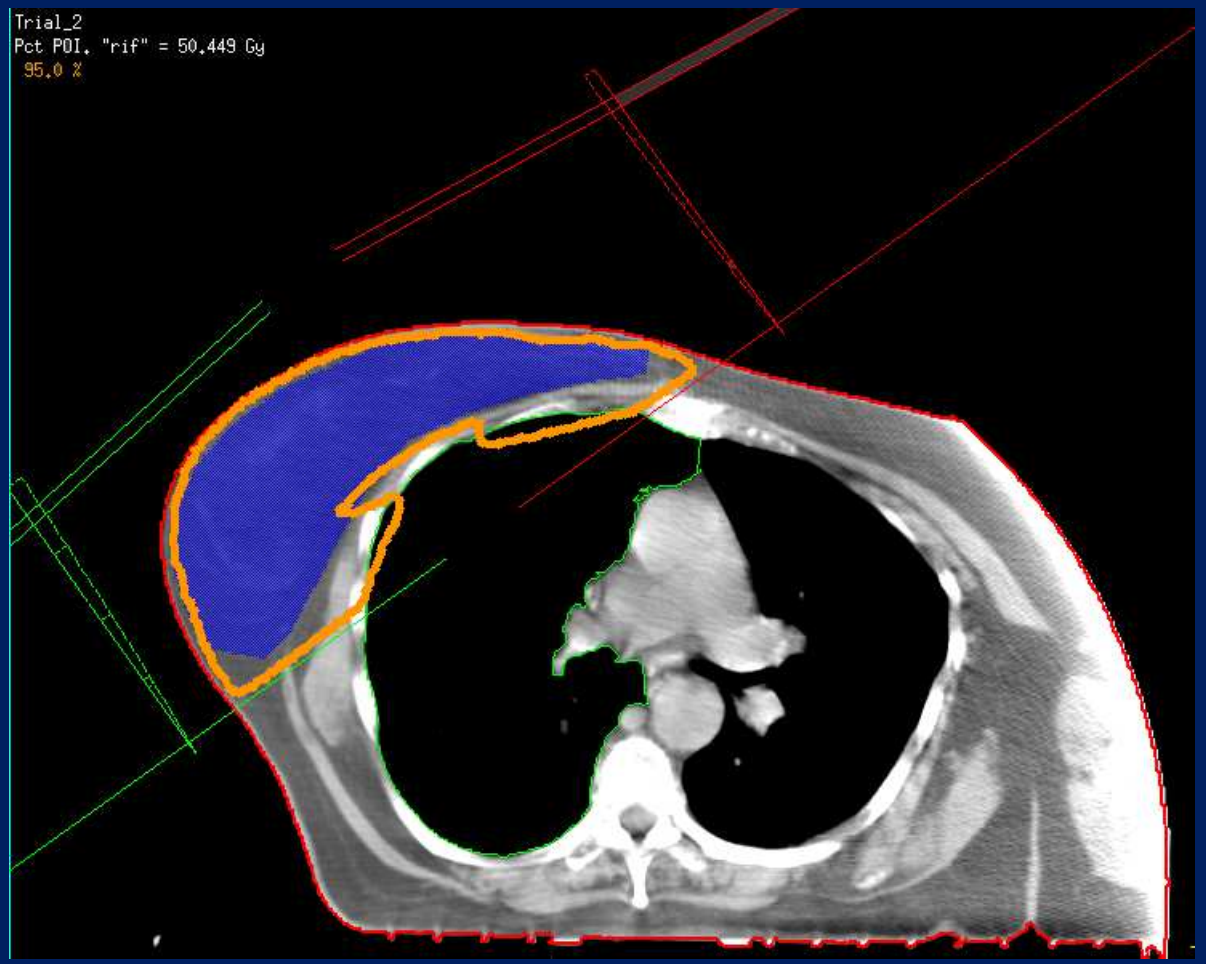
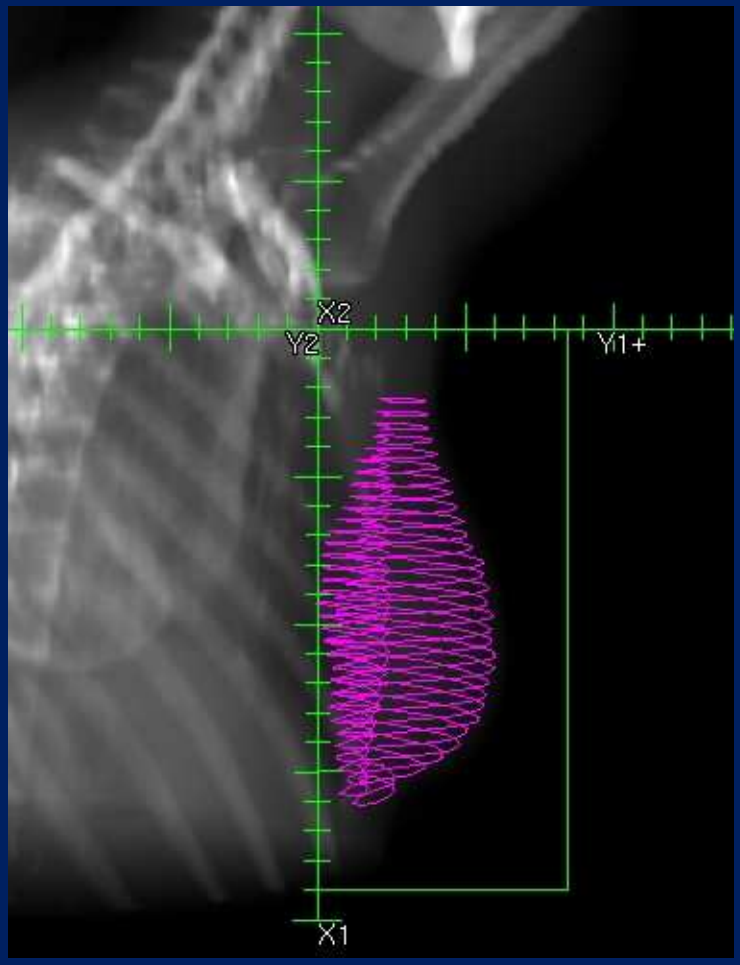

Trial_2
Pct POI, "rif" = 50.449 Gy
95.0 %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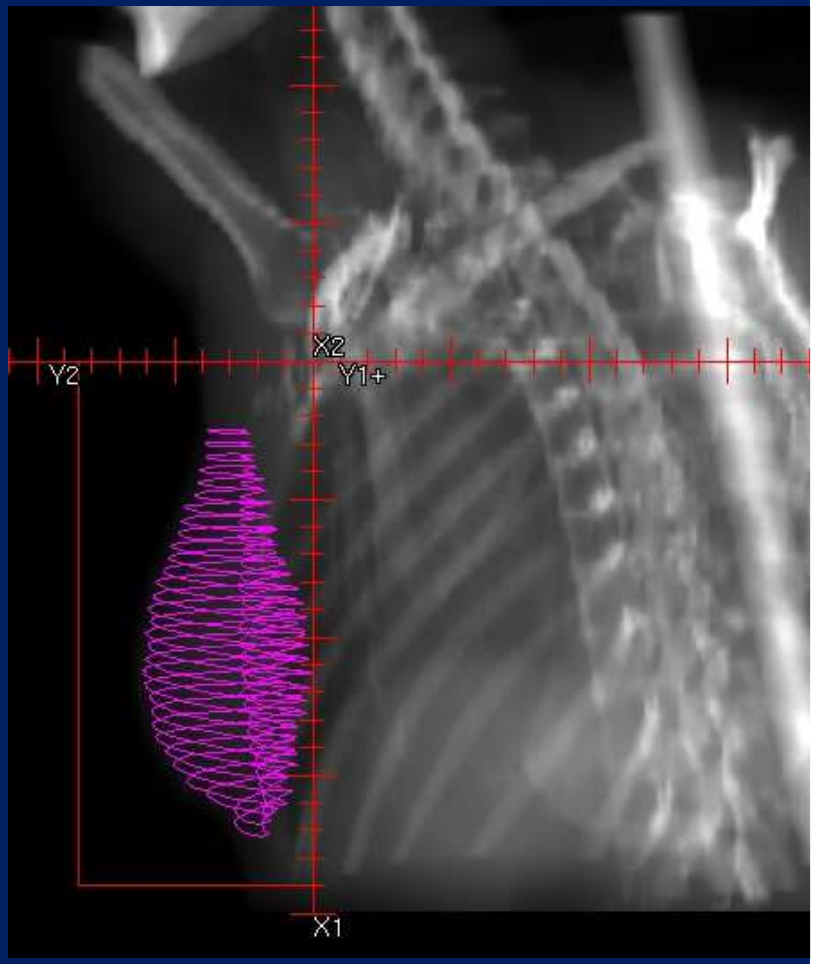
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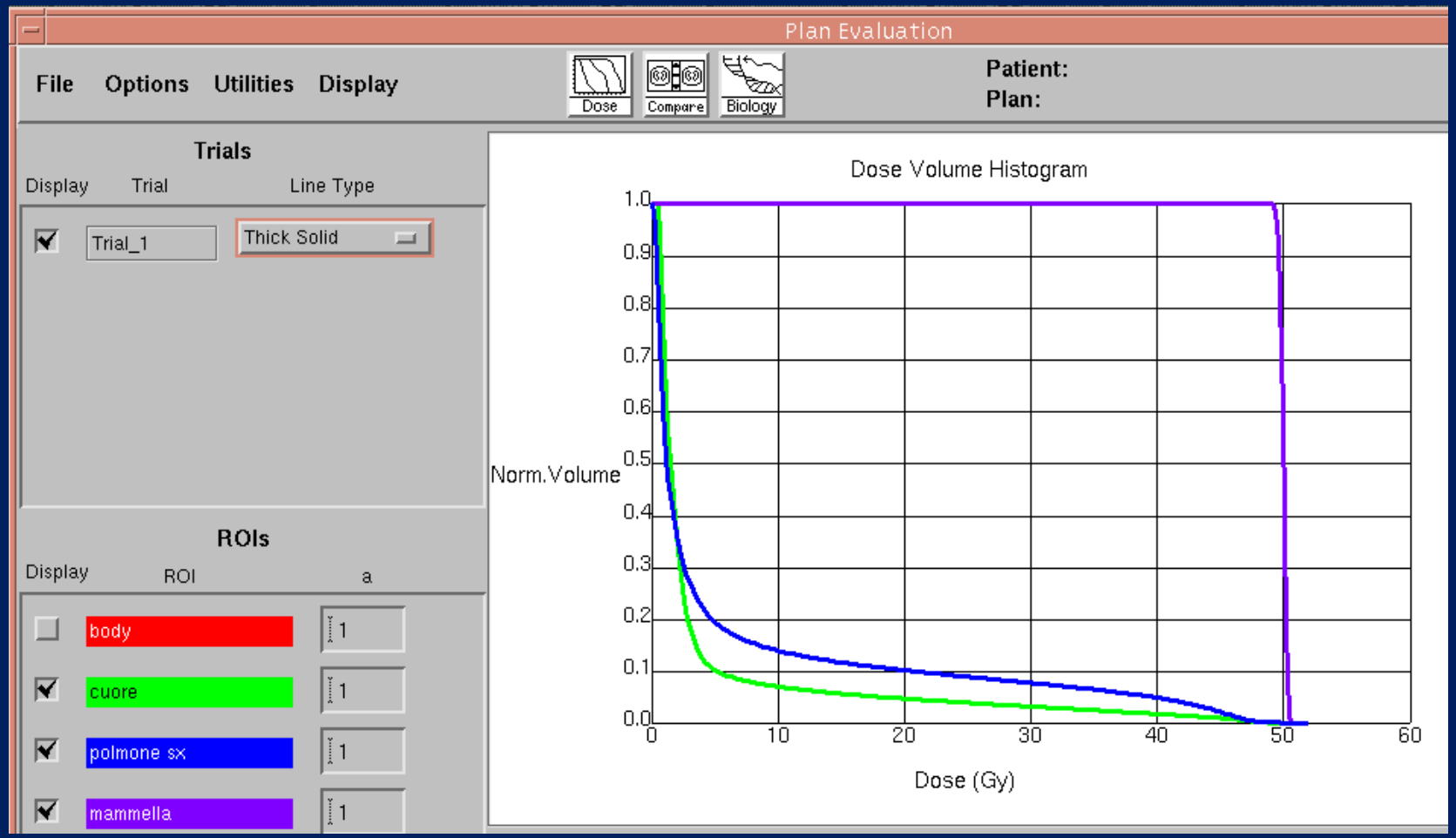
Plan Evaluation
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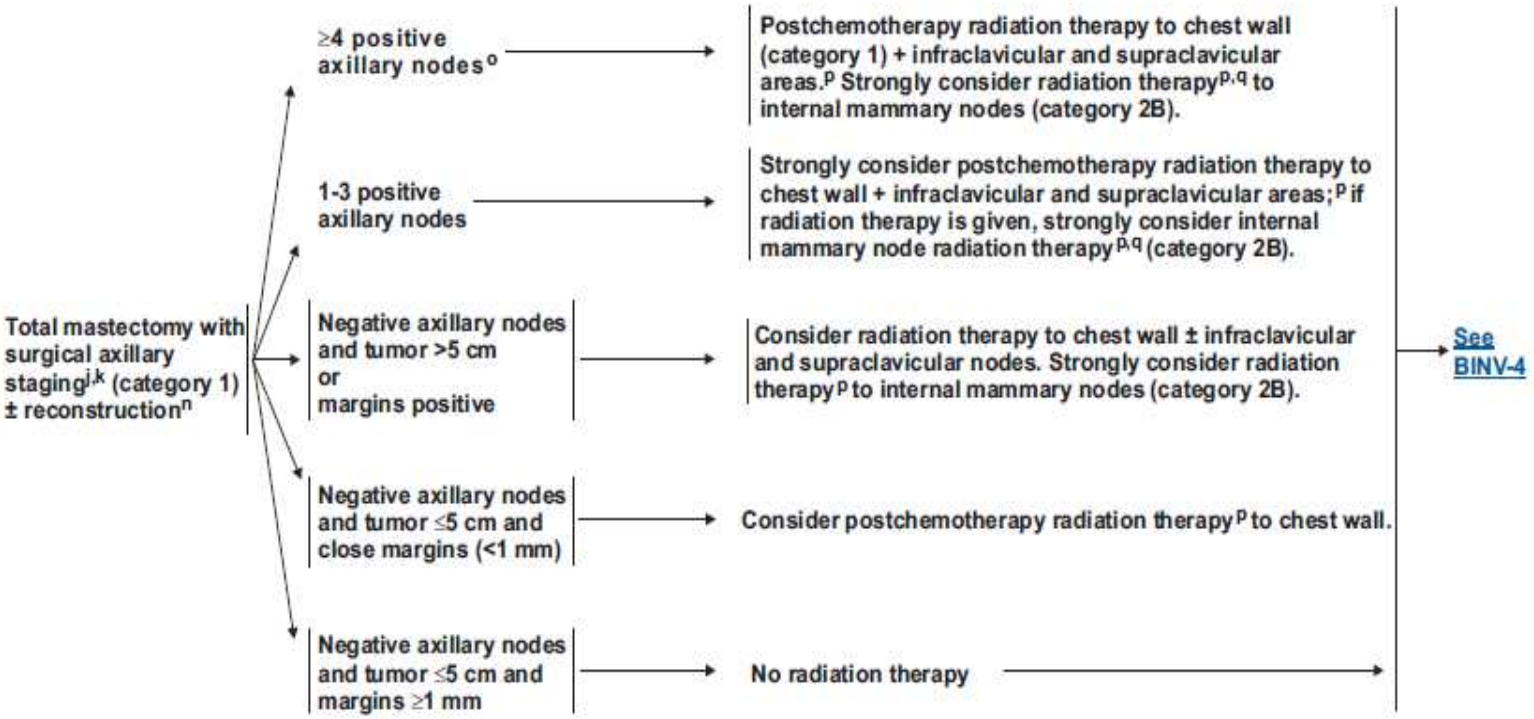
10
20
30
40
50
60
Dose (Gy)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



[j] See Surgical Axillary Staging (BINV-D).

[k] See Axillary Lymph Node Staging (BINV-E) and Margin Status in Infiltrating Carcinoma (BINV-F).

[n] See Principles of Breast Reconstruction Following Surgery (BINV-H).

[o] Consider imaging for systemic staging, including diagnostic CT or MRI, bone scan, and optional FDG PET/CT (category 2B) (See BINV-1).

[p] See Principles of Radiation Therapy (BINV-I).

[q] Radiation therapy should be given to the internal mammary lymph nodes that are clinically or pathologically positive, otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where radiation therapy is delivered to the internal mammary lymph nodes.

Radioterapia dopo mastectomia

- L'indicazione ad un trattamento radiante dopo mastectomia è attualmente limitata alle pazienti ad alto rischio di recidiva loco-regionale, quali quelle con malattia T3-4, margini di resezione positivi, invasione della fascia pettorale, invasione della cute e dei linfatici del derma.

- Nelle pazienti con 4 o più linfonodi ascellari positivi il trattamento viene effettuato sulla parete toracica e sulla fossetta sovraclaveare omolaterale, con possibile estensione all'ascella omolaterale solo nel caso in cui si sospetti residuo di malattia.

RT POST MASTECTOMIA

STUDI RANDOMIZZATI

STUDIO	N° Pz	RLR		DFS		OS	
		RT-	RT+	RT-	RT+	RT-	RT+
DBCG 82b NEJM 1997	1708	32%	9% p< 0.001	34%	48% p< 0.001	45%	54% p< 0.001
BCT NEJM 1997	318	33%	13% p = 0.003	33%	50% p = 0.007	46%	54% p = 0.07
DBCG 82c Lancet 1999	1375	35%	8% p< 0.001	24%	36% p< 0.001	36%	45% p = 0.03
BCT update JNCI 2005	318	39%	13% p < 0.001			37%	47% p = 0.03

LE META-ANALISI

	N° pz (N° studi)	Follow-up (anni)	RLR (%) RT+	RLR (%) RT-	OS (%) RT+	OS (%) RT-
EBCTCG *Lancet, 2000*	20.000 (40)		8.8 10.4	27.2° 30.1°°	37.1 p = 0.06	35.9
			p< 0.00001			
Van de Steene *Radiother Oncol, 2000*	7840 (7)	8-10			p = 0.004	
Whelan *JCO, 2000*	6367 (18)	7.5-14.5	p < 0.00001		p = 0.004	

° a 10 anni, °° a 20 anni

Stopping metastases at their source.

Samuel Hellman. NEJM 337:996-997, 1997.

Le metastasi a distanza originano dalla malattia microscopica loco-regionale residua alla chirurgia.

La RT e la terapia sistemica hanno bersagli differenti:

- ✓ **la RT controlla la malattia microscopica loco-regionale**
- ✓ **la terapia sistemica agisce prevalentemente sulle micrometastasi**

Radioterapia dei drenaggi linfatici

Stazioni Linfonodali

- ✓ Sovraclaveare
- ✓ Mammaria Interna
- ✓ Ascella

TOSSICITÀ TRATTAMENTO RADIANTE

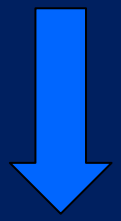
Durante il trattamento radiante i tessuti sani sono inevitabilmente esposti alle radiazioni

Le pazienti possono manifestare sintomi che sono espressione del danno ai tessuti sani

Il processo patologico del danno indotto dalle radiazioni inizia immediatamente dopo l'esposizione, ma le manifestazioni cliniche ed istologiche possono evidenziarsi settimane, mesi od anni dopo il trattamento.

Rischio tossicità

Trattamento convenzionale



buon controllo di malattia

bassa tossicità

SITUAZIONI A RISCHIO DI AUMENTATA TOSSICITÀ

Particolare conformazione anatomica:

petto escavato

mammella voluminosa

Eccessivo volume cardiaco e polmonare nel campo di irradiazione

IMRT

IMRT deve essere considerata lo standard per l'irradiazione della ghiandola mammaria?

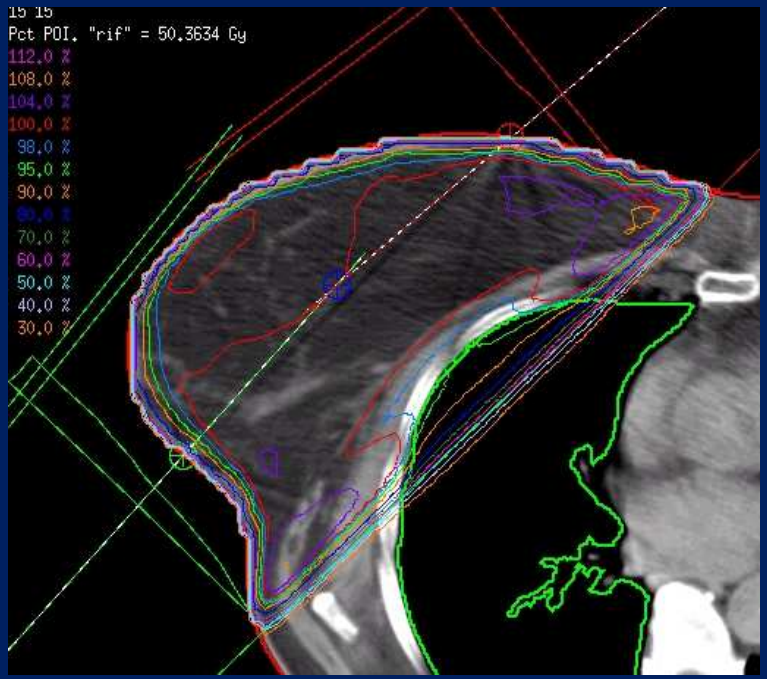
NO

RISERVATA A SITUAZIONI PARTICOLARI

LIMITAZIONI CAMPI TANGENZIALI STANDARD

Le aree di sovradosaggio sono a rischio di tossicità

mammella voluminosa



Particolare conformazione anatomica
mammella voluminosa

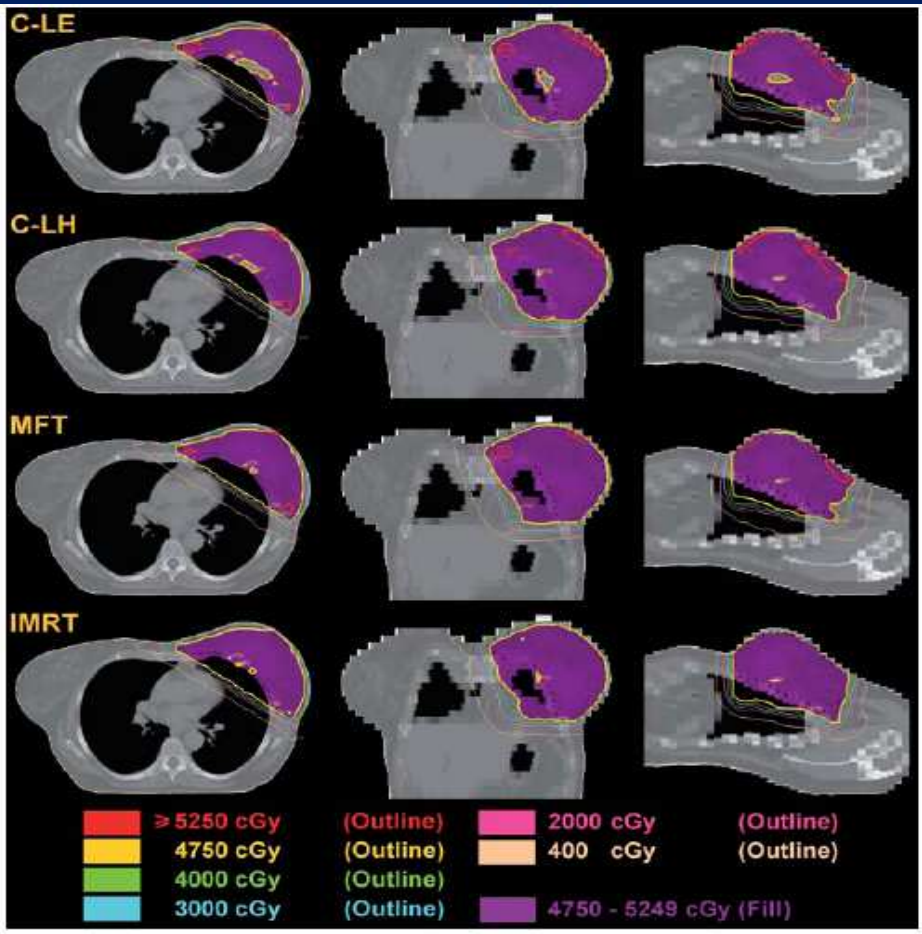
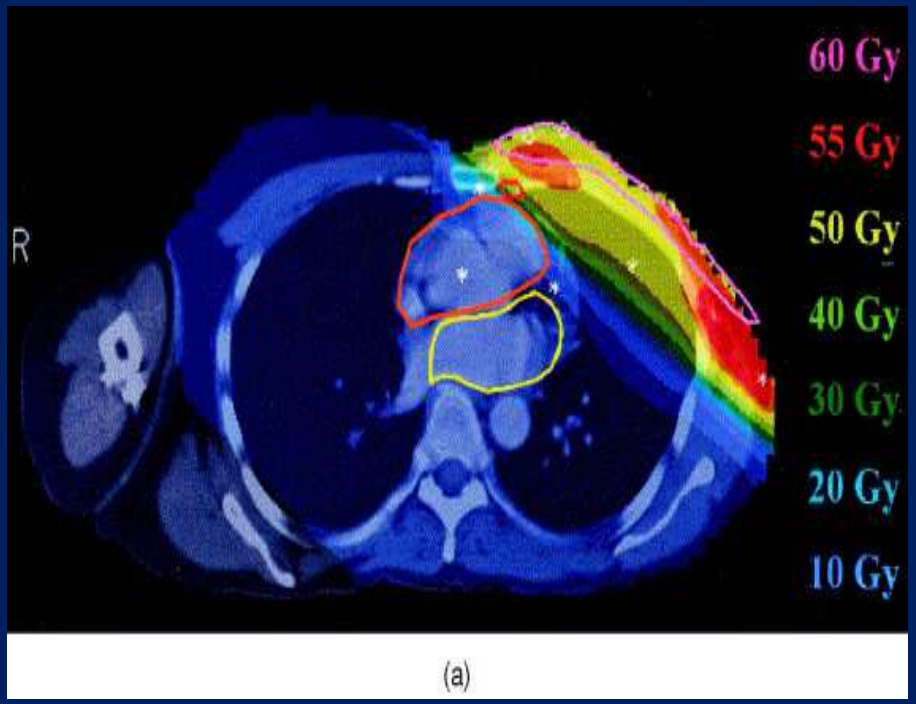


Figure 2. Isodose distribution in axial, coronal, and sagittal views comparing the four techniques for one typical patient from the cohort of ten patients in the study. IMRT results in the most homogeneous dose distribution.

Abo.Madyan et al.,
Stranhelnther Onkol 2008

IMRT PARETE TORACICA E DRENAGGI LINFONODALI



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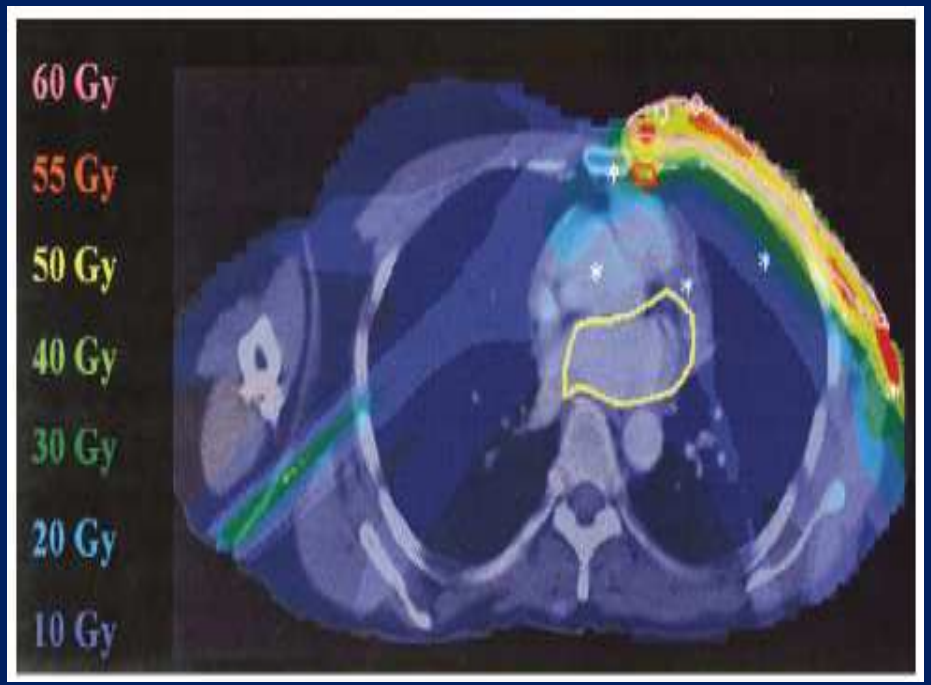
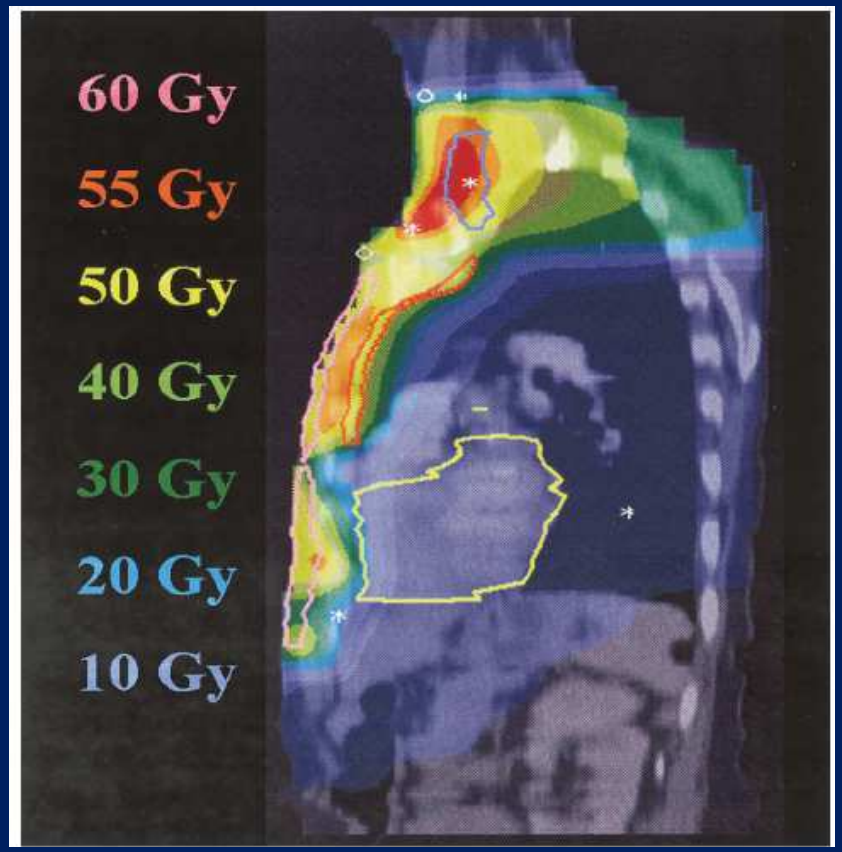
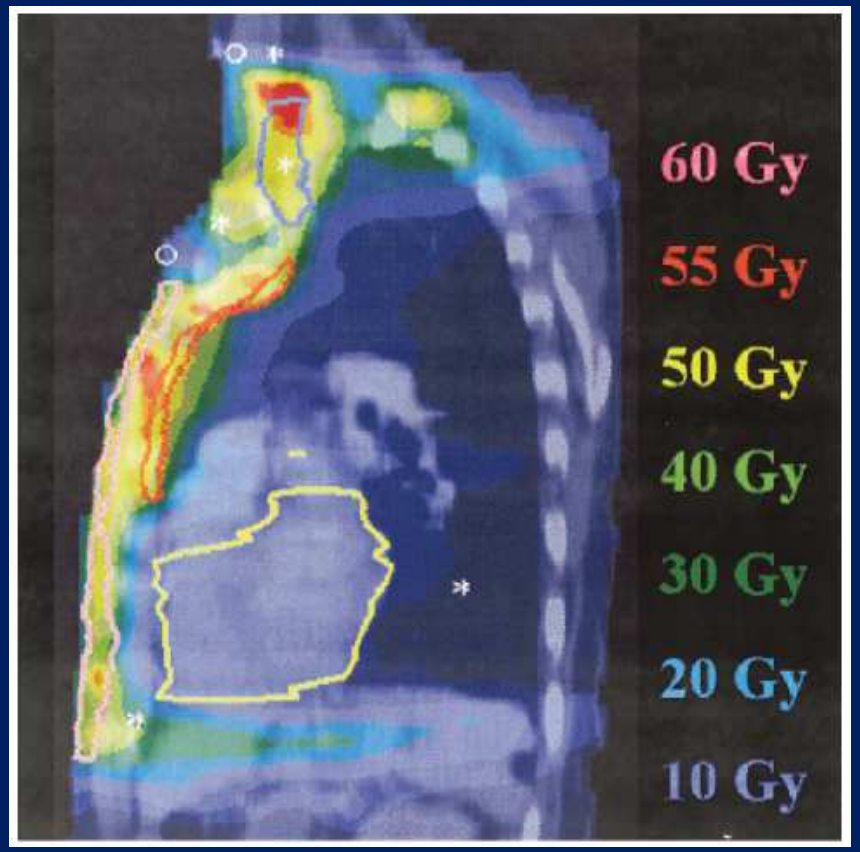


IMRT

Krueger et al, IJROBP 2003

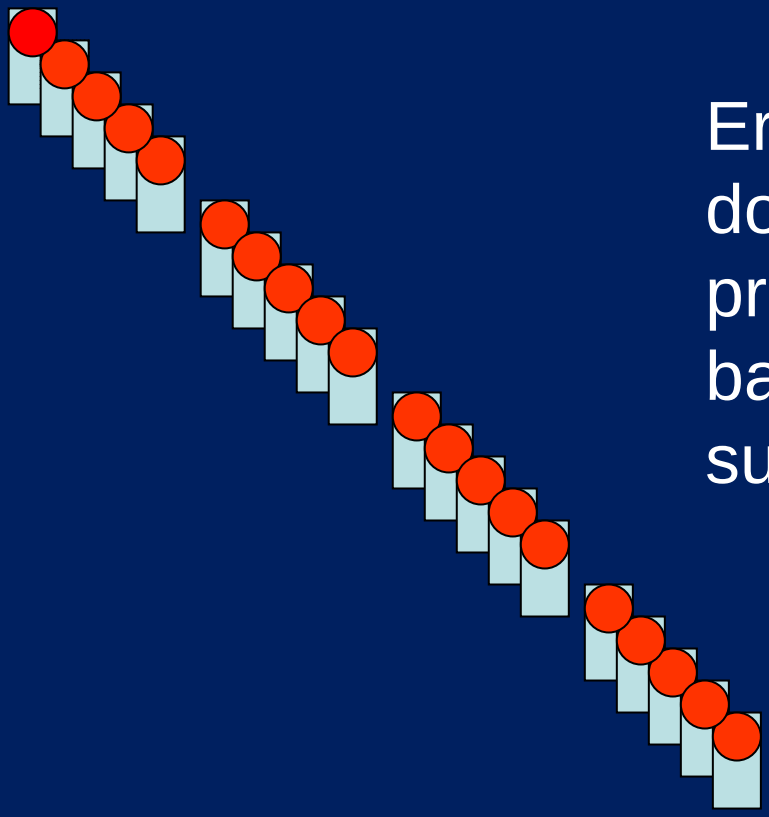
IMRT PARETE TORACICA E DRENAGGI LINFONODALI





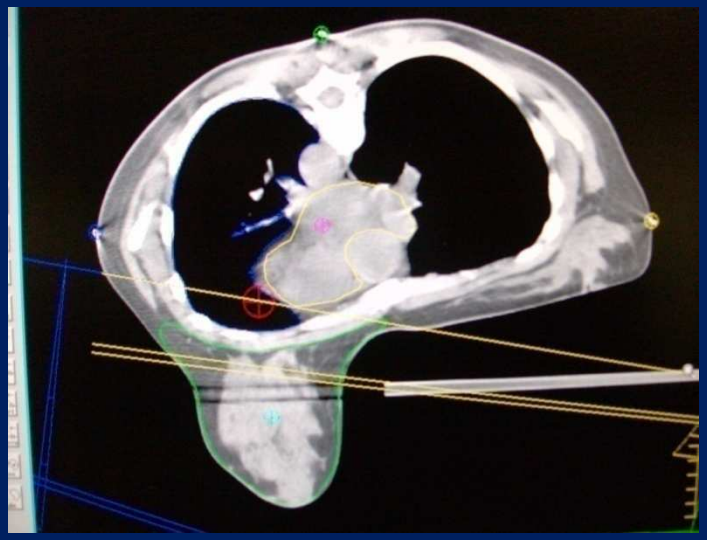
Krueger et al, IJROBP 2003

Boost Simultaneo Integrato (SIB)



Eroga simultaneamente una dose alta alla malattia primitiva e una dose più bassa alla malattia subclinica

RT MAMMELLA CON PAZIENTE IN POSIZIONE PRONA



INDICAZIONI:

mammelle voluminose e pendule

impossibilità a mantenere la posizione supina

particolari condizioni anatomiche della parete toracica per ridurre quanto più possibile l'irradiazione polmonare e cardiaca

RT MAMMELLA CON PAZIENTE IN POSIZIONE PRONA

RISULTATI

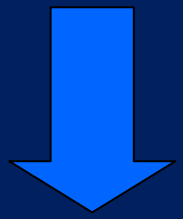
migliore omogeneità della distribuzione di dose rispetto alla posizione supina

riduzione del volume polmonare compreso nel campo di irradiazione

non sicuri vantaggi sono stati osservati sicuri vantaggi sul risparmio di volume cardiaco

la tossicità cutanea acuta e cronica risulta paragonabile o inferiore al trattamento in posizione supina

IRRADIAZIONE PARZIALE



Trattamento radiante effettuato, dopo chirurgia conservativa, sulla sede del tumore primitivo con un margine di sicurezza di 1-2 cm

CARCINOMA INIZIALE DELLA MAMMELLA

La chirurgia conservativa seguita da radioterapia sull'intera ghiandola è il trattamento lo standard

Veronesi *et al. NEJM* 1981;305:6-11
Fisher *et al.* *NEJM* 1985;312:665-673
Blichert-Toft et al. *JNCI Monogr* 1992; 11:19-25.
Jacobson et al. *N EJ M* 1995;332:907-911.
Van Dongen et al. *J NCI Monogr* 1992; 11:15-18.
Arriagada *et al.* *J CO* 1996; 14:1558-1564.
Veronesi *et al. NEJM* 2002;347:1227-1232.
Fisher et *al. NEJM* 2002;347:1233-1241.
1990 National Institute for Health Consensus Conference. Treatment of early-stage breast cancer. JAMA 265:391-395, 1991.

Molte pazienti affette da carcinoma iniziale della mammella non possono ricevere il trattamento conservativo per:

- **Carenza di strutture di Radioterapia**
- **Motivi logistici**
- **Problemi di tempo**

Sono pertanto sottoposte a:

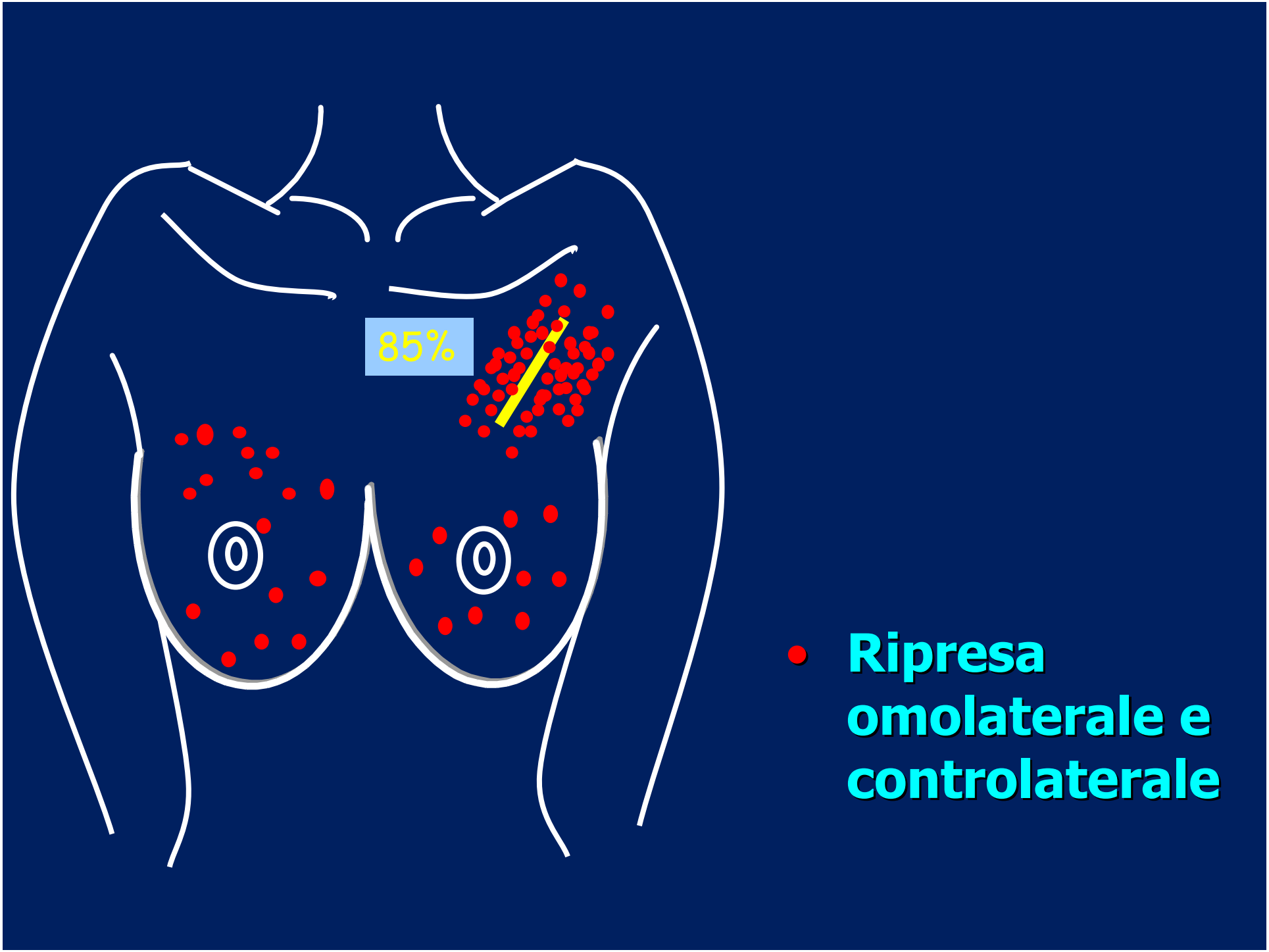
- **mastectomia**
- **sola chirurgia conservativa senza radioterapia**

IRRADIAZIONE PARZIALE DELLA MAMMELLA DOPO CHIRURGIA CONSERVATIVA

- Somministra una dose/frazione elevata di RT sulla cavità escissionale con 1-2 cm di margine.
- Il trattamento è effettuato in 4-5 giorni o, nel caso della IORT, durante la seduta operatoria.

RAZIONALE

- L’80%-90% delle recidive si manifesta nel letto tumorale.
- L’irradiazione dell’intera mammella potrebbe essere superflua in gruppi selezionati di pazienti.
- La supposta maggiore efficacia del trattamento dovrebbe ridurre il rischio di recidiva nel letto tumorale.



- **Ripresa omolaterale e controlaterale**

VANTAGGI

- Riduce la durata totale del trattamento.
- Aumenta la possibilita’ che molte donne possano essere sottoposte a chirurgia conservativa.
- Migliora la qualità di vita delle pazienti.
- Elimina problemi di timing con la chemioterapia

SELEZIONE DELLE PAZIENTI

- Pazienti con minimo rischio di malattia multicentrica

MAMMOGRAFIA

- Tumori con bassa probabilità di estensione microscopica 1-2 cm oltre il primitivo

CONSENSUS STATEMENT

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

BENJAMIN D. SMITH, M.D.,[*†] DOUGLAS W. ARTHUR, M.D.,[‡] THOMAS A. BUCHHOLZ, M.D.,[†] BRUCE G. HAFFTY, M.D.,[§] CAROL A. HAHN, M.D.,[‖] PATRICIA H. HARDENBERGH, M.D.,[¶] THOMAS B. JULIAN, M.D.,[#] LAWRENCE B. MARKS, M.D.,[**] DORIN A. TODOR, PH.D.,[‡] FRANK A. VICINI, M.D.,[††] TIMOTHY J. WHELAN, M.D.,[‡‡] JULIA WHITE, M.D.,[§§] JENNIFER Y. WO, M.D.,[‖‖] AND JAY R. HARRIS, M.D.[¶¶]

Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 4, pp. 987–1001, 2009

Radiotherapy and Oncology 94 (2010) 264–273

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

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 Guinot[i], 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

ASTRO RECOMMENDATIONS

Table 2. Patients "suitable" for APBI if all criteria are present

Factor	Criterion
Patient factors	
Age	≥60 y
BRCA1/2 mutation	Not present
Pathologic factors	
Tumor size	≤2 cm*
T stage	T1
Margins	Negative by at least 2 mm
Grade	Any
LVSI	No†
ER status	Positive
Multicentricity	Unicentric only
Multifocality	Clinically unifocal with total size ≤2.0 cm‡
Histology	Invasive ductal or other favorable subtypes§
Pure DCIS	Not allowed
EIC	Not allowed
Associated LCIS	Allowed
Nodal factors	
N stage	pN0 (i^-, i^+)
Nodal surgery	SN Bx or ALND‖
Treatment factors	
Neoadjuvant therapy	Not allowed

Table 3. "Cautionary" group: Any of these criteria should invoke caution and concern when considering APBI

Factor	Criterion
Patient factors	
Age	50–59 y
Pathologic factors	
Tumor size	2.1–3.0 cm*
T stage	T0 or T2
Margins	Close (<2 mm)
LVSI	Limited/focal
ER status	Negative†
Multifocality	Clinically unifocal with total size 2.1–3.0 cm‡
Histology	Invasive lobular
Pure DCIS	≤3 cm
EIC	≤3 cm

Table 4. Patients "unsuitable" for APBI outside of a clinical trial if any of these criteria are present

Factor	Criterion
Patient factors	
Age	<50 y
BRCA1/2 mutation	Present
Pathologic factors	
Tumor size*	>3 cm
T stage	T3-4
Margins	Positive
LVSI	Extensive
Multicentricity	Present
Multifocality	If microscopically multifocal >3 cm in total size or if clinically multifocal
Pure DCIS	If >3 cm in size
EIC	If >3 cm in size
Nodal factors	
N stage	pN1, pN2, pN3
Nodal surgery	None performed
Treatment factors	
Neoadjuvant therapy	If used

Smith, IJROBP 2

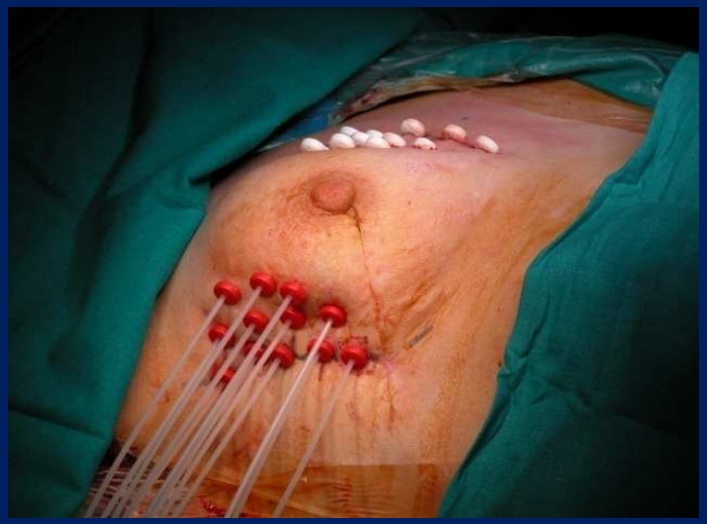
ESTRO RECOMMENDATIONS

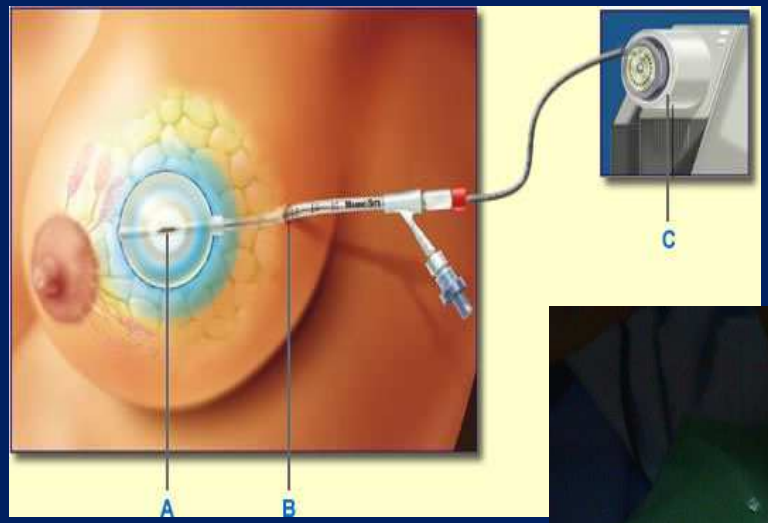
Table 8
GEC-ESTRO recommendations on patient selection for accelerated partial-breast irradiation.

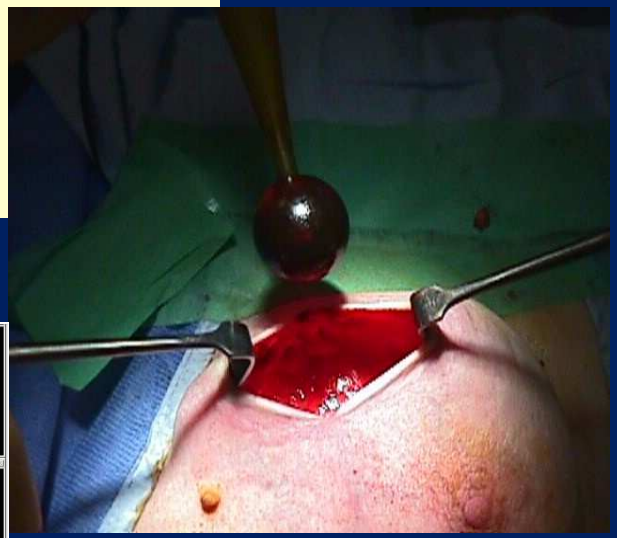
Characteristic	A/low-risk group – good candidates for APBI	B/intermediate-risk group – possible candidates for APBI	C/high-risk group – contraindication for APBI
Patient age	>50 years	>40–50 years	⩽40 years
Histology	IDC, mucinous, tubular, medullary, and colloid cc.	IDC, ILC, mucinous, tubular, medullary, and colloid cc	–
ILC	Not allowed	Allowed	–
Associated LCIS	Allowed	Allowed	–
DCIS	Not allowed	Allowed	–
HG	Any	Any	–
Tumour size	pT1–2 (⩽30 mm)	pT1–2 (⩽30 mm)	pT2 (>30 mm), pT3, pT4
Surgical margins	Negative (⩾2 mm)	Negative, but close (<2 mm)	Positive
Multicentricity	Unicentric	Unicentric	Multicentric
Multifocality	Unifocal	Multifocal (limited within 2 cm of the index lesion)	Multifocal (>2 cm from the index lesion)
EIC	Not allowed	Not allowed	Present
LVI	Not allowed	Not allowed	Present
ER, PR status	Any	Any	–
Nodal status	pN0 (by SLNB or ALND[a])	pN1mi, pN1a (by ALND[a])	pNx; ⩾pN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

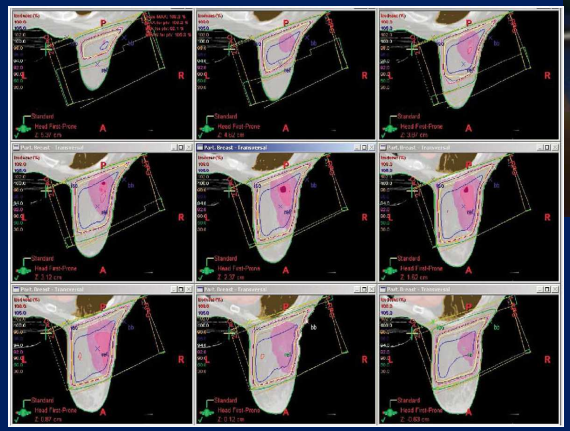
Polgàr, R&O 201

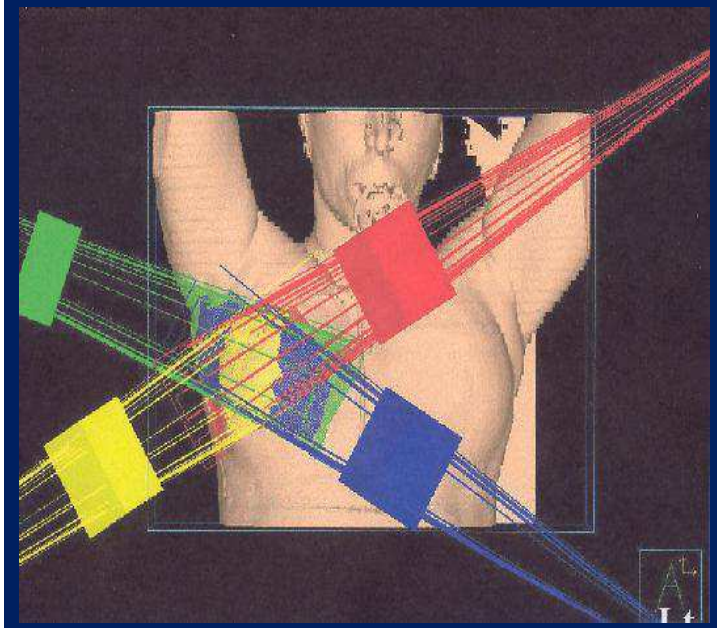
PBI

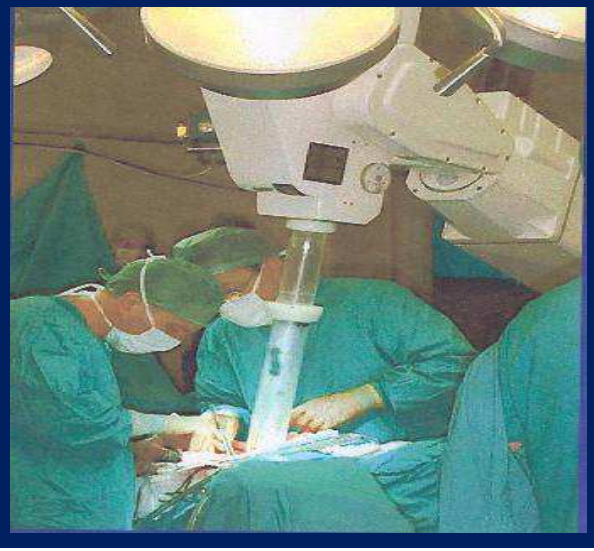


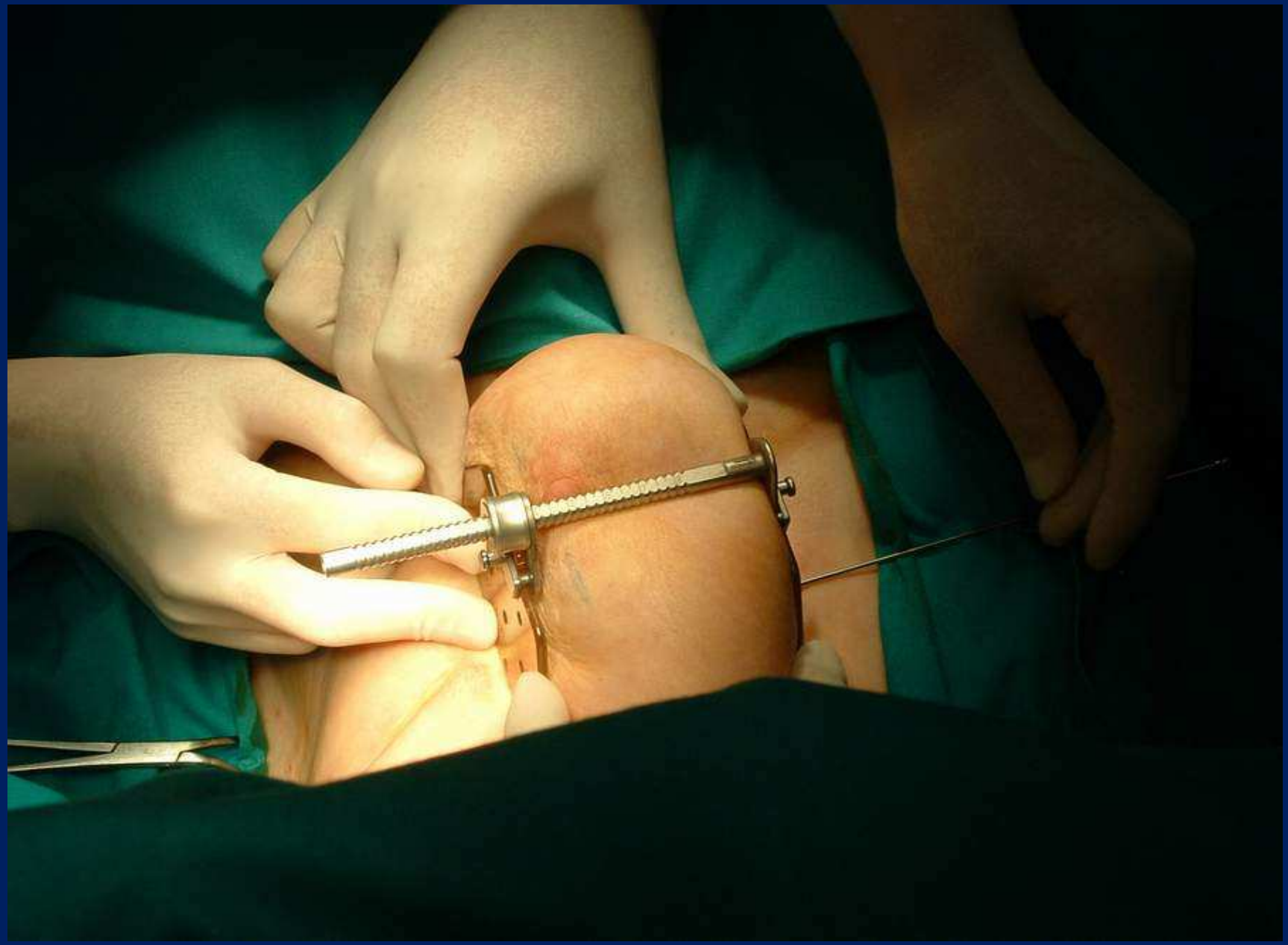


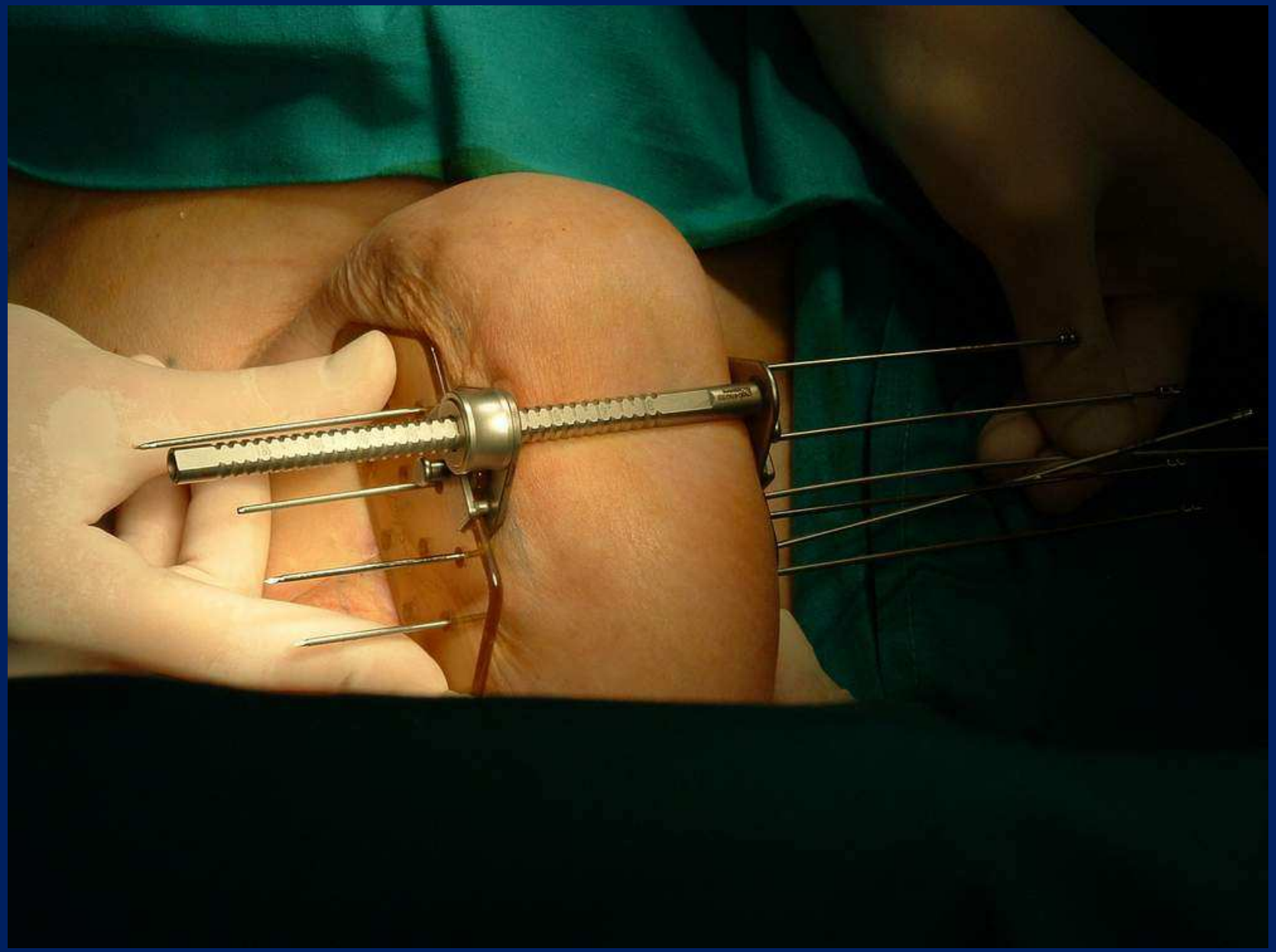


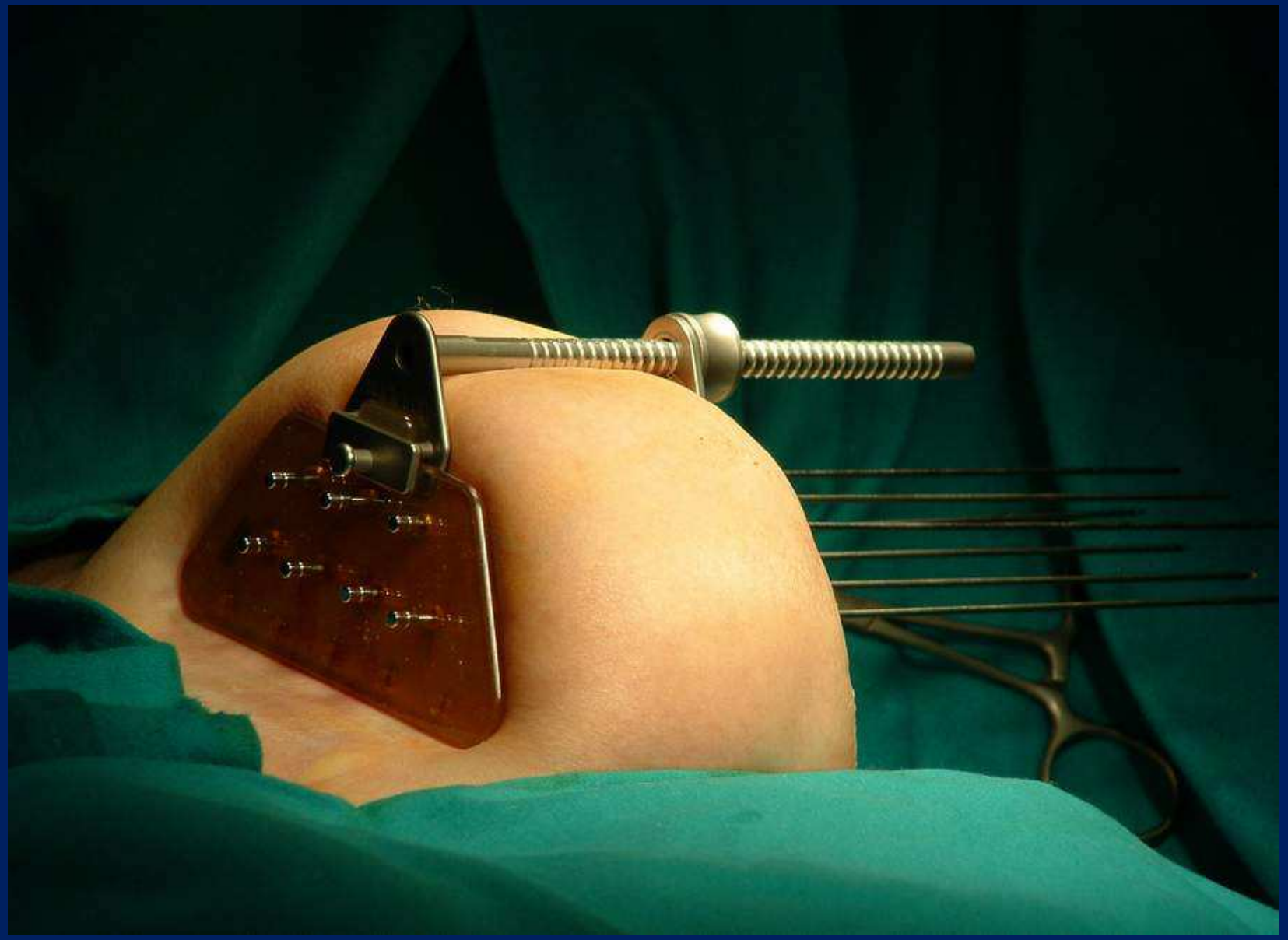


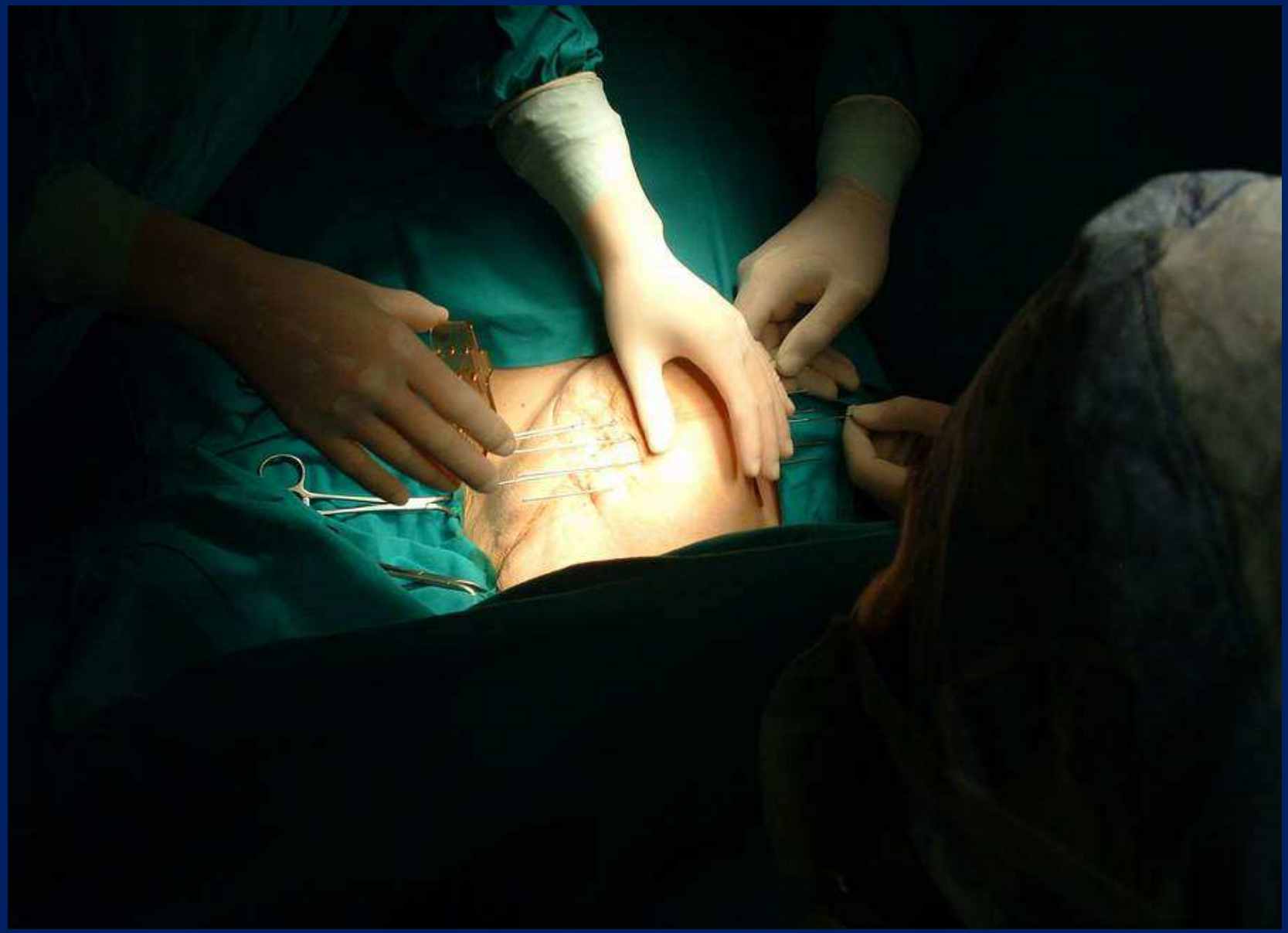


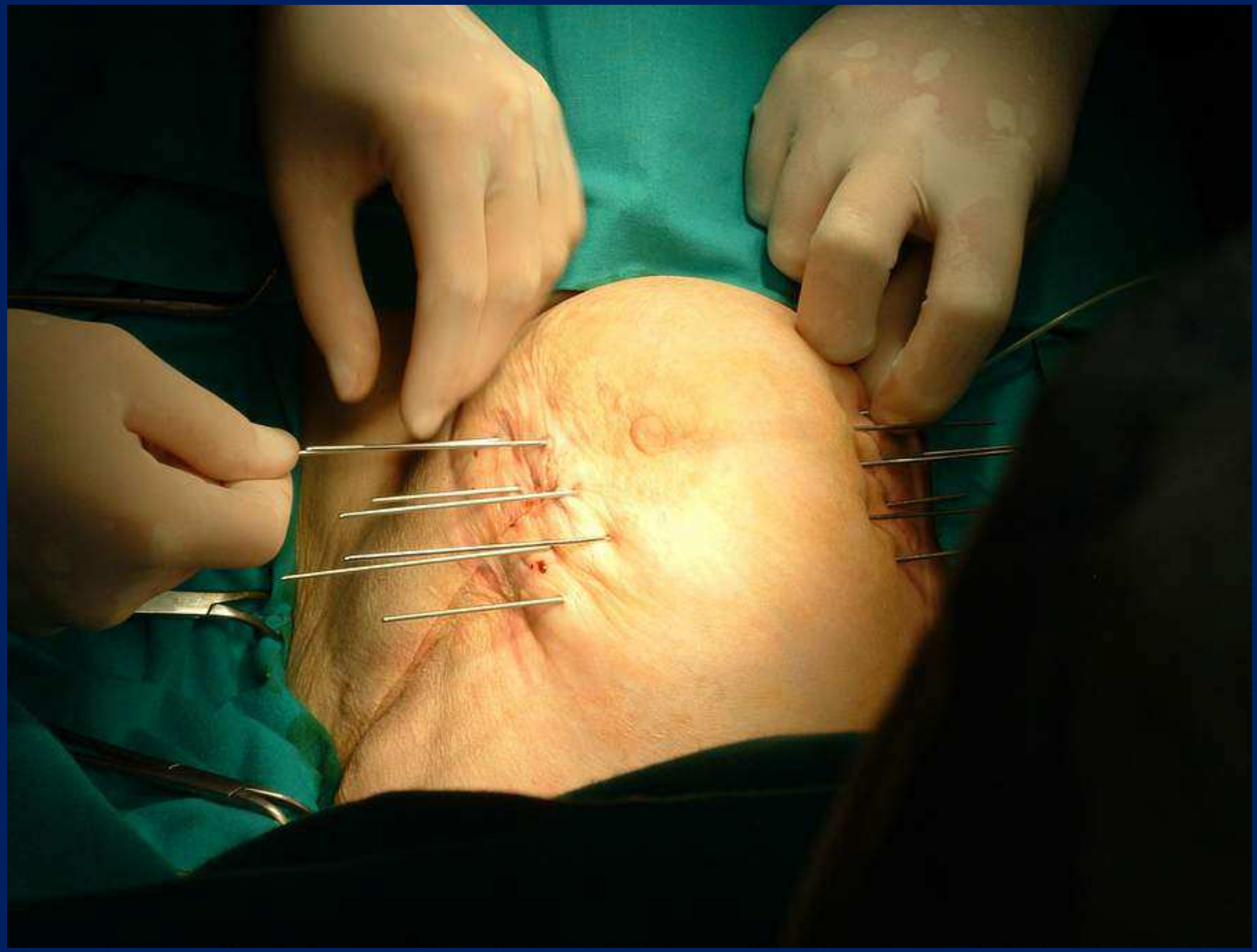


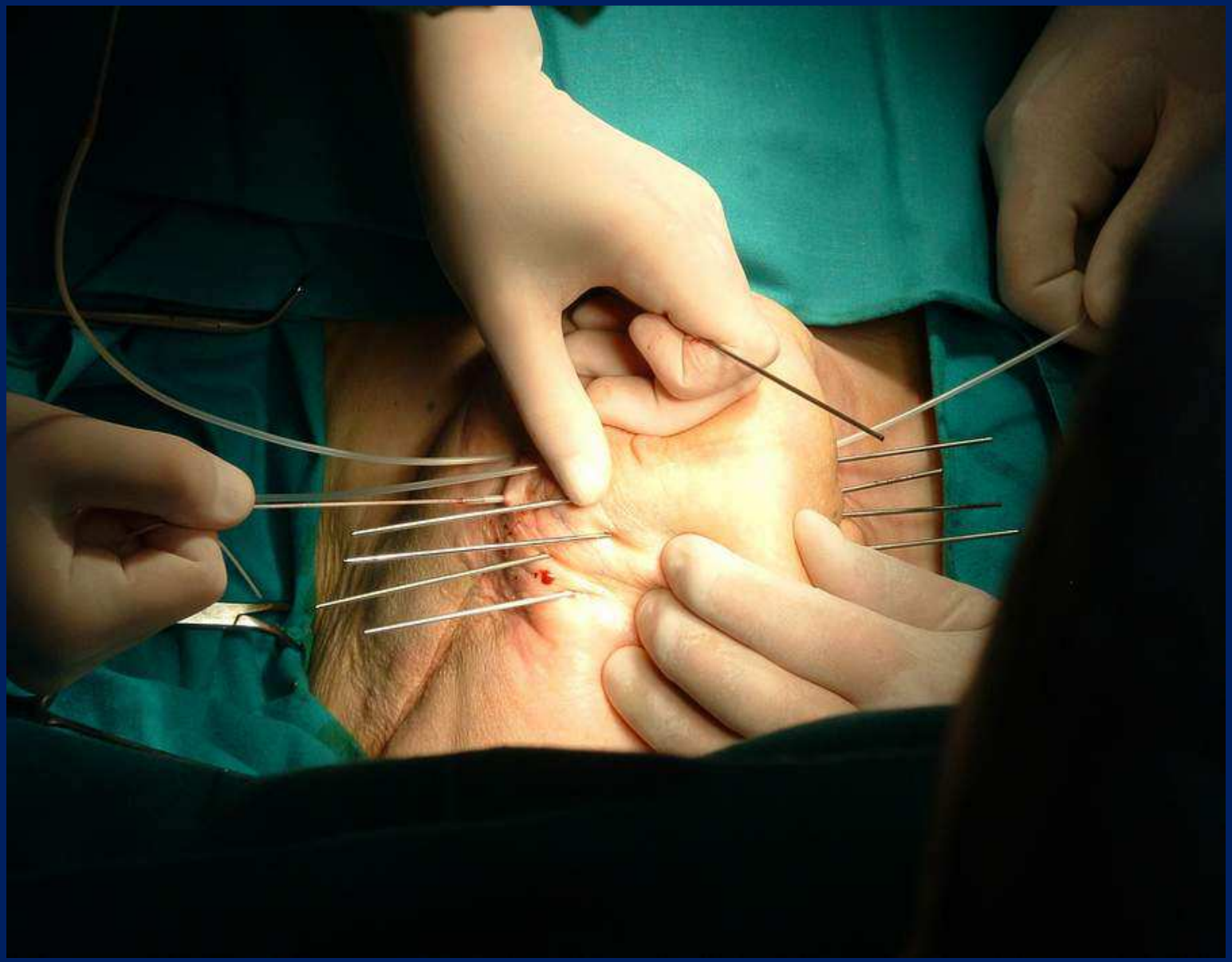


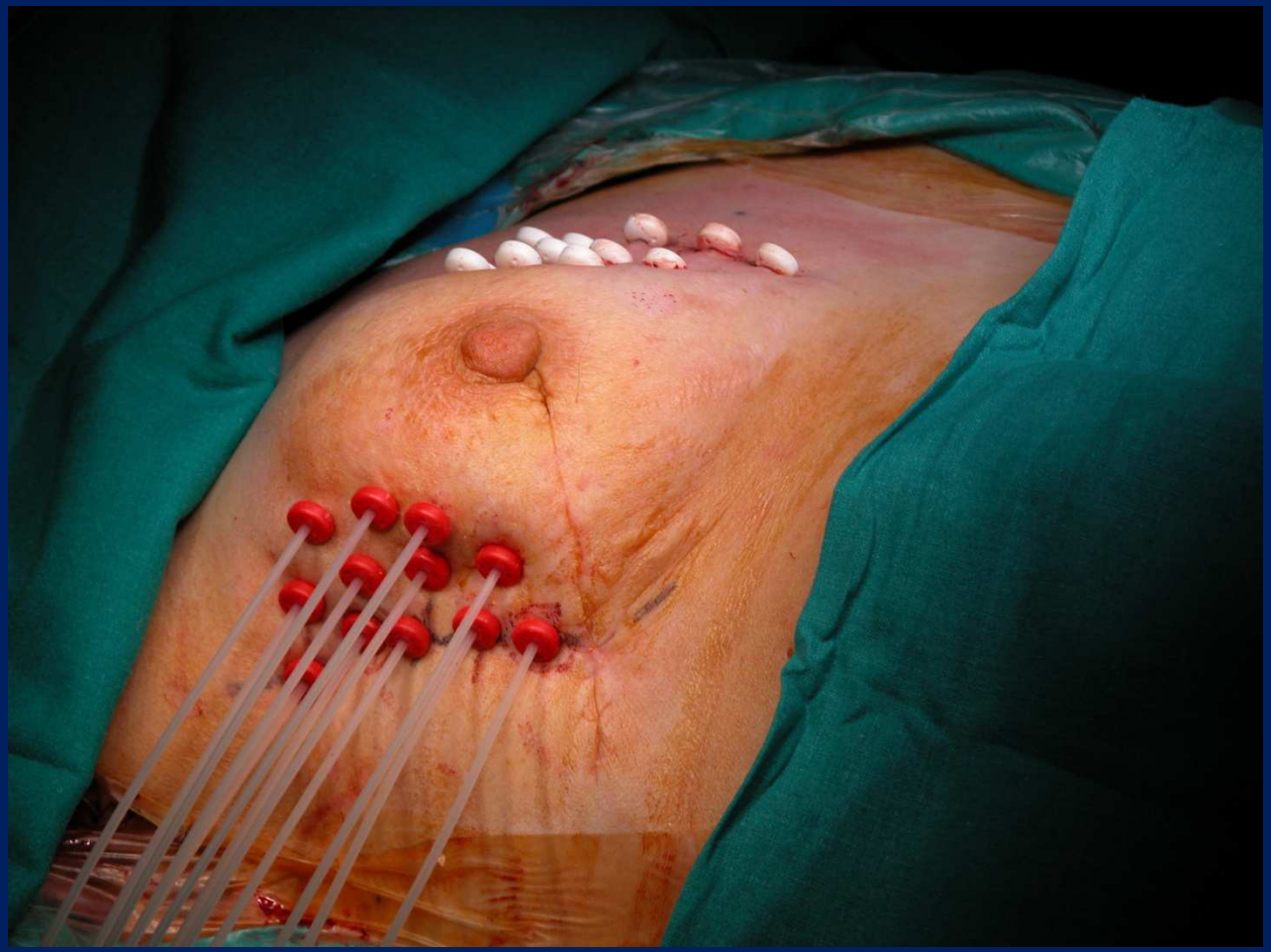


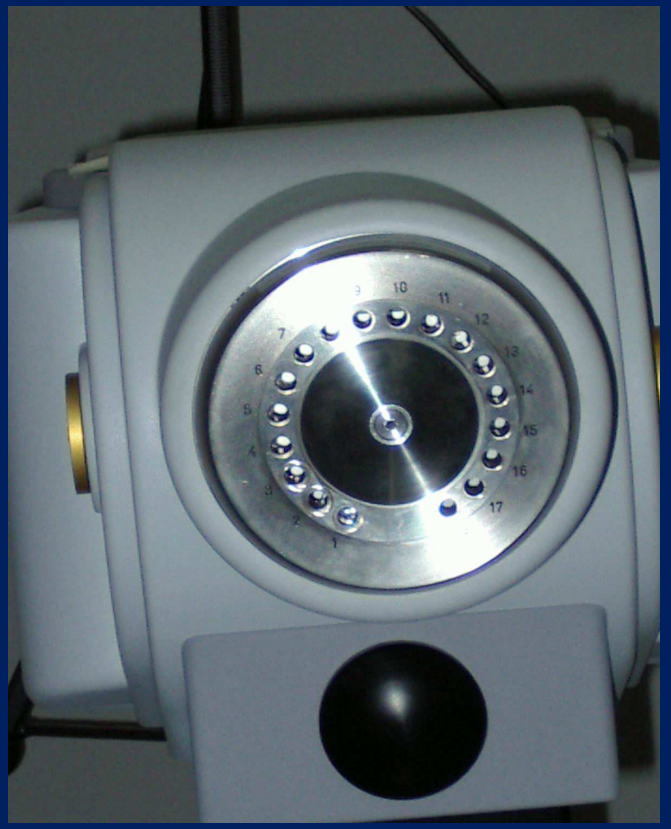




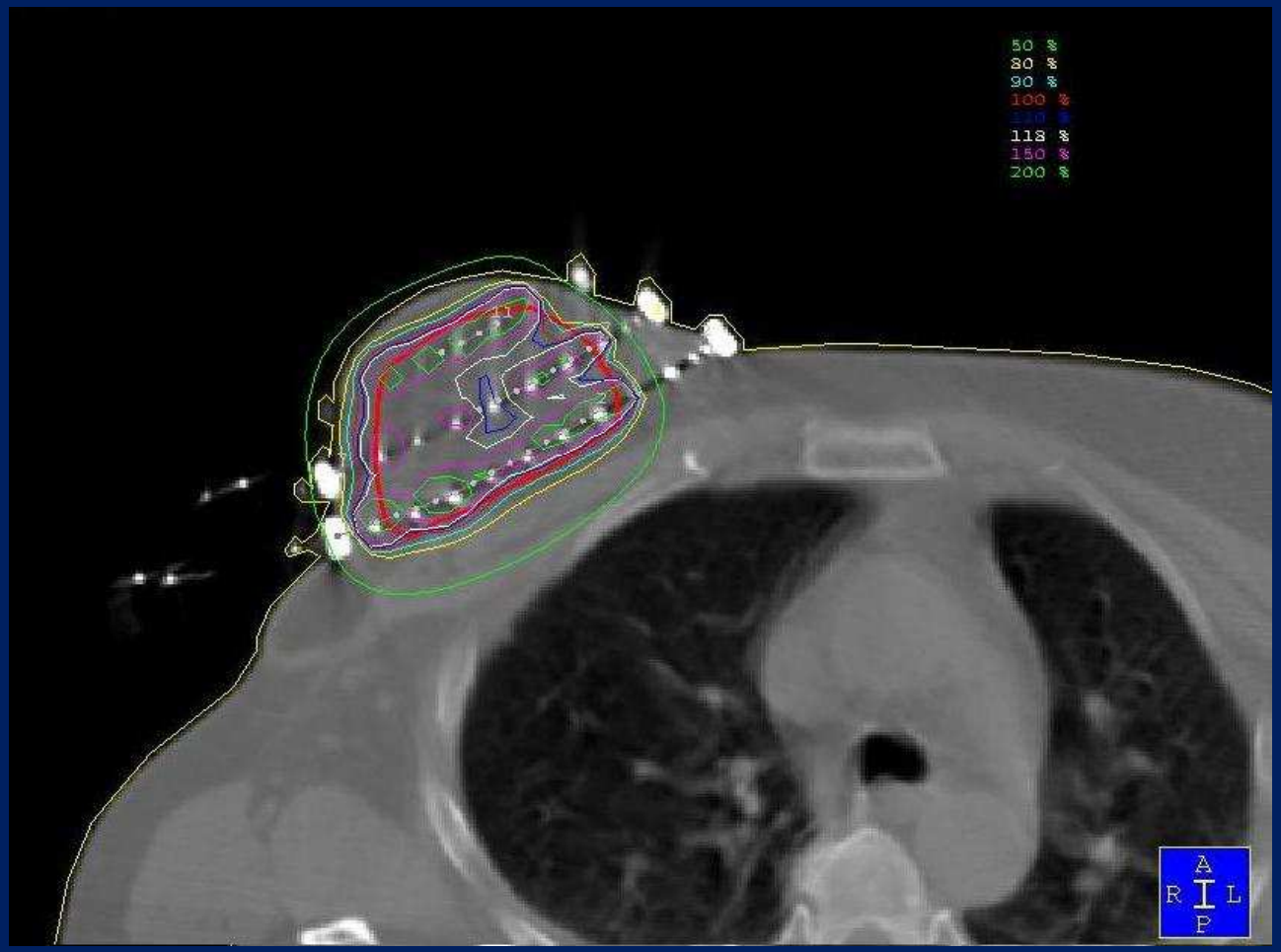




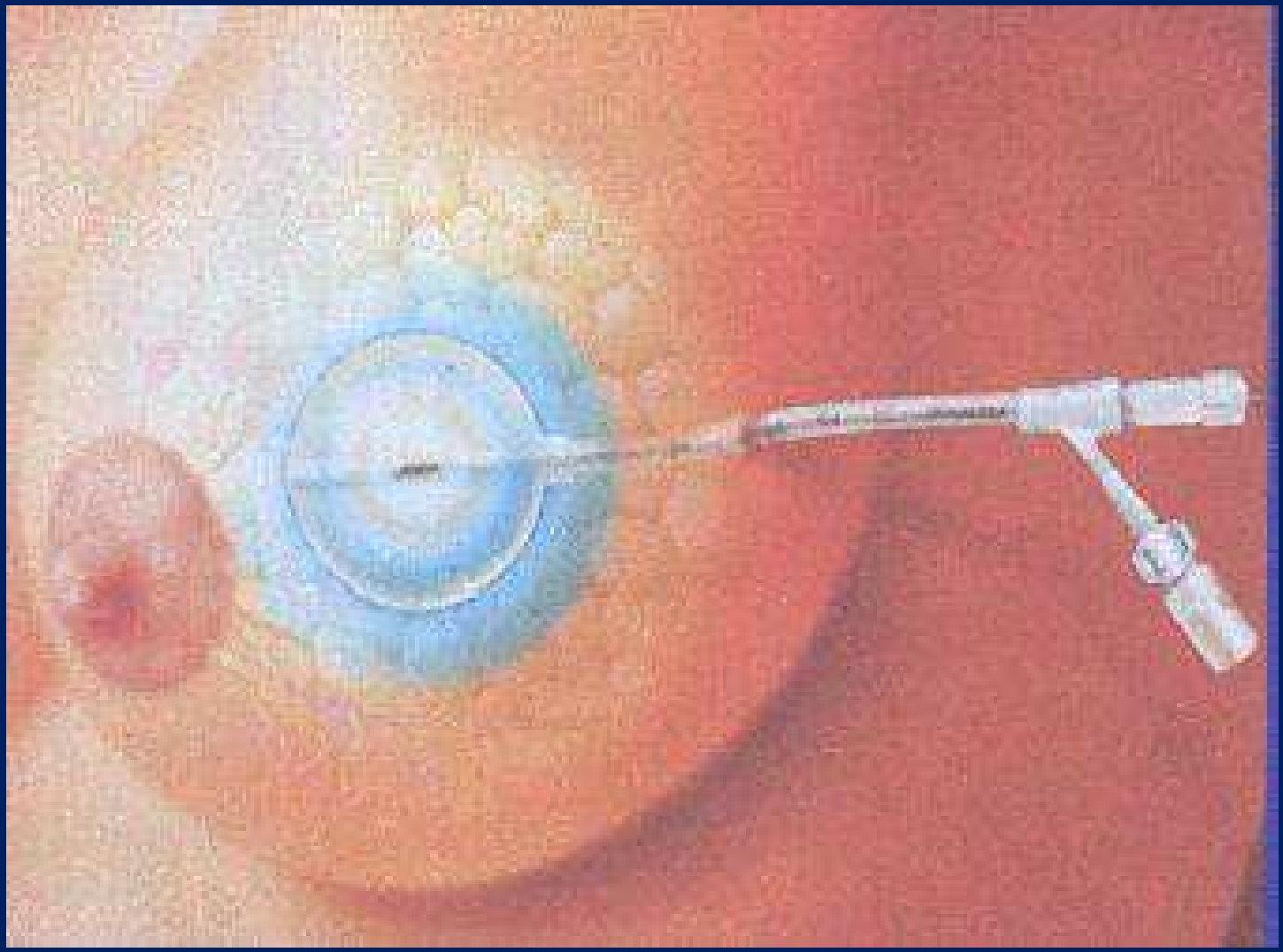


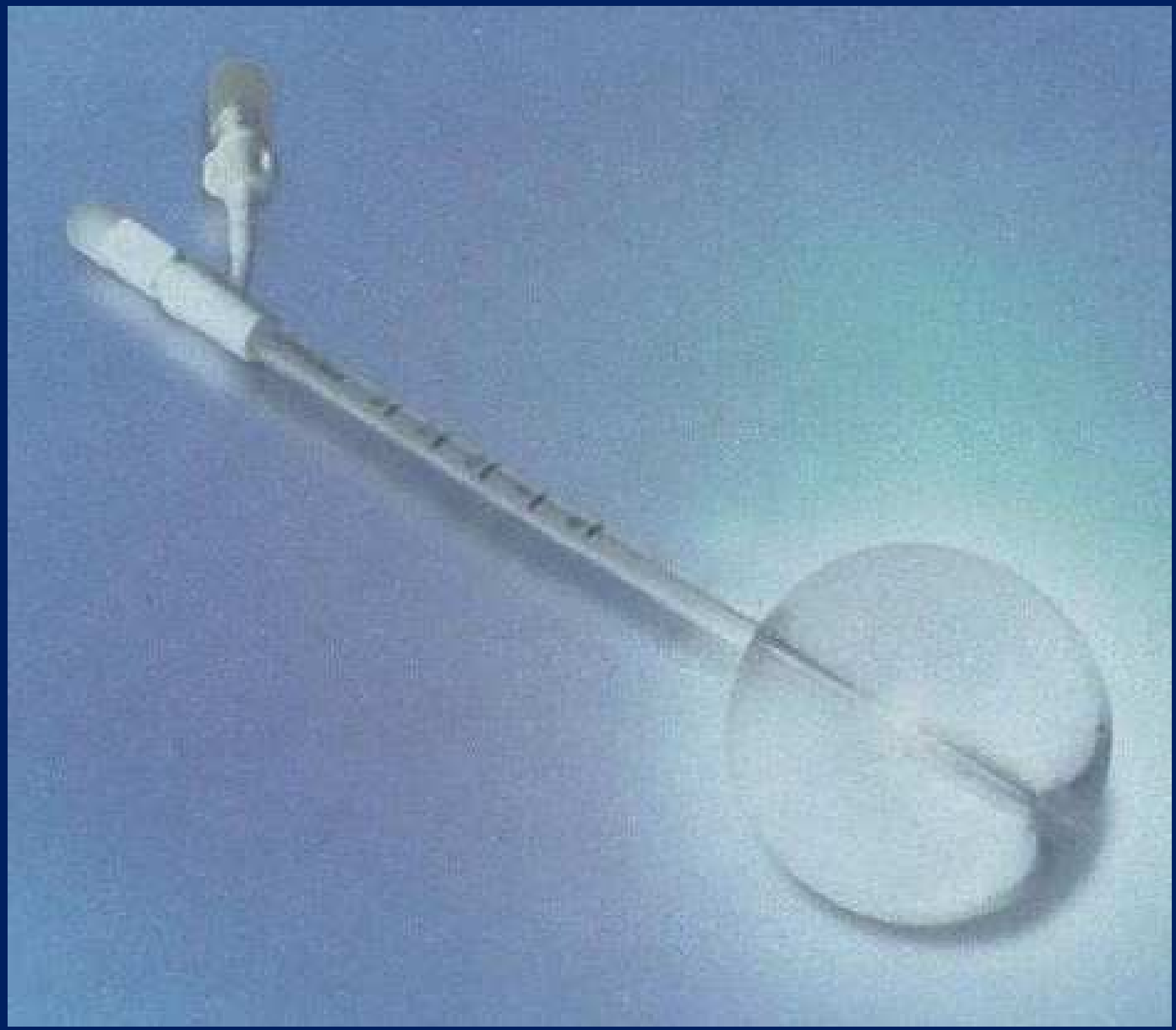


MICROSELECTRON HDR ^{192}Ir REMOTE AFTERLOADING SYSTEM (NUCLEOTRON, THE NEDERLANDS)

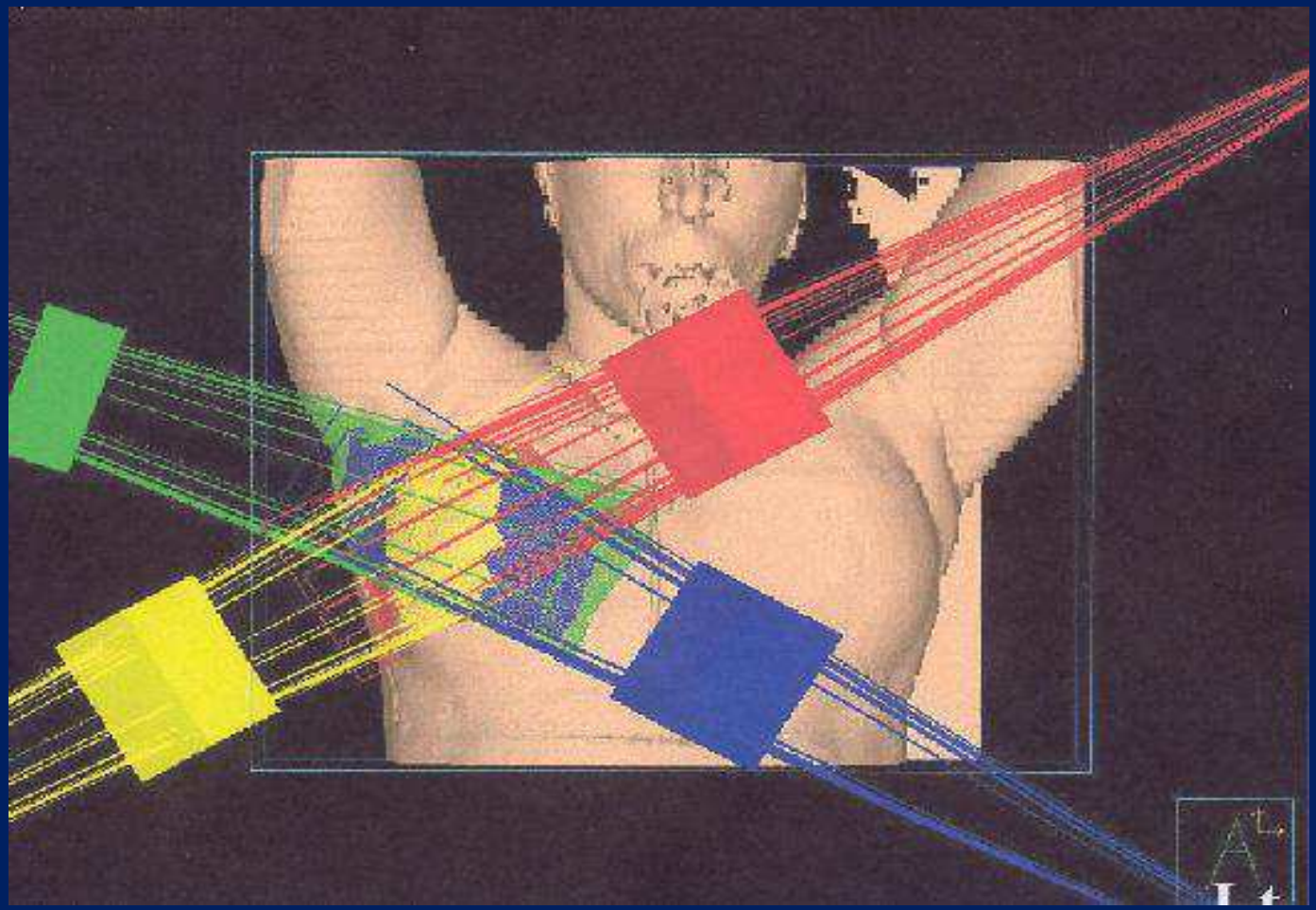

50 %
80 %
90 %
100 %
118 %
150 %
200 %
A
R L
P

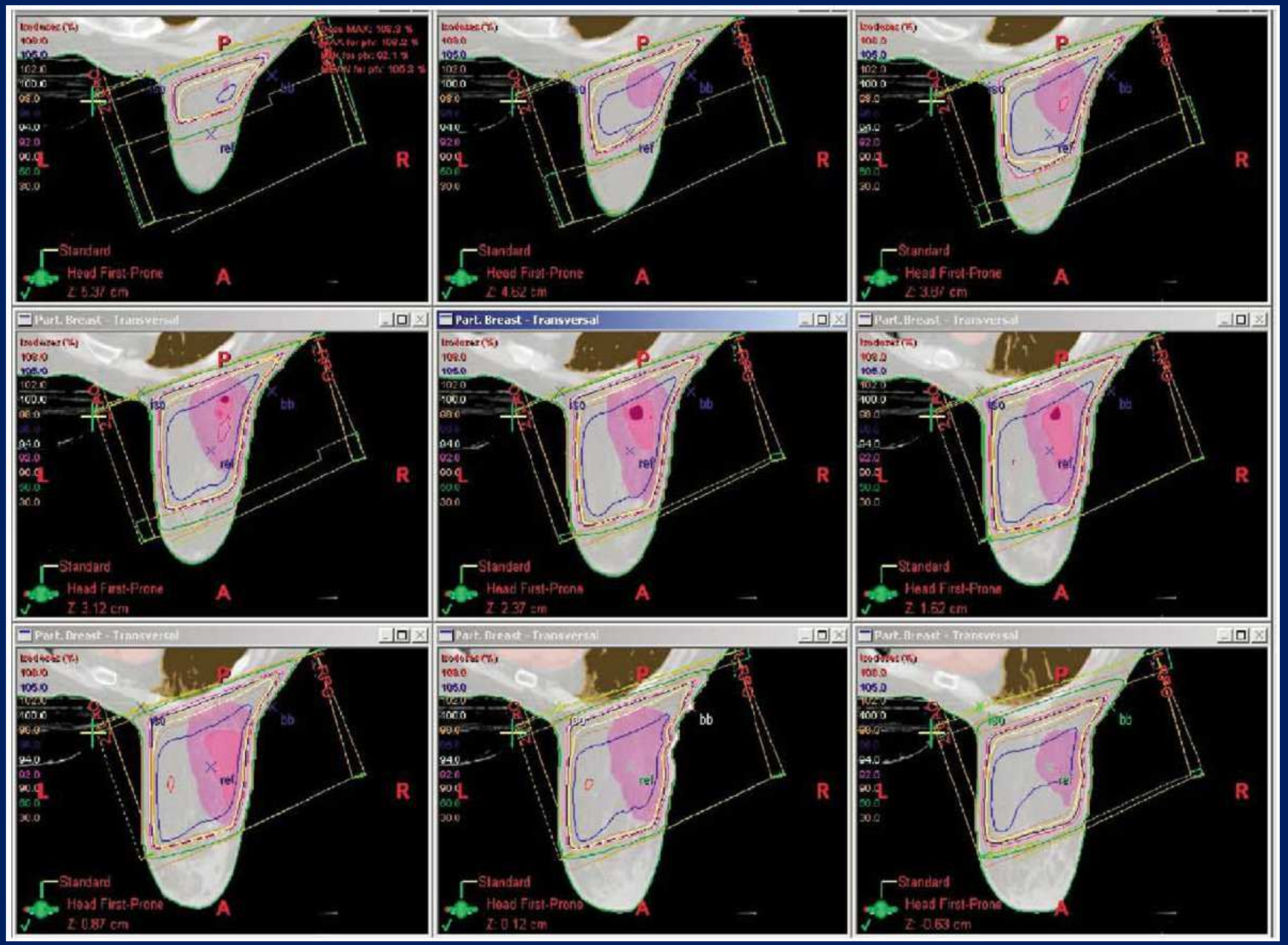
MAMMOSITE





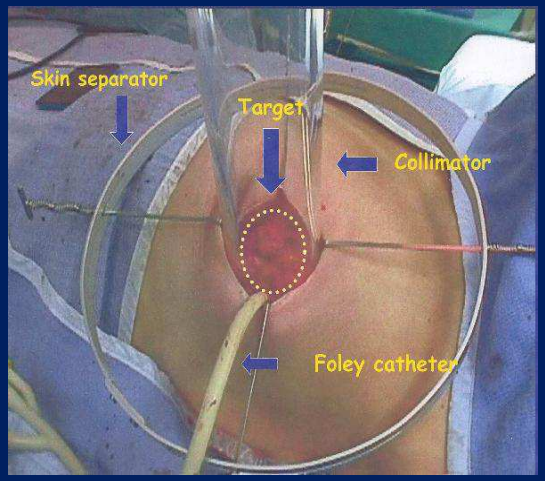
RADIOTERAPIA CONFORMAZIONALE 3D

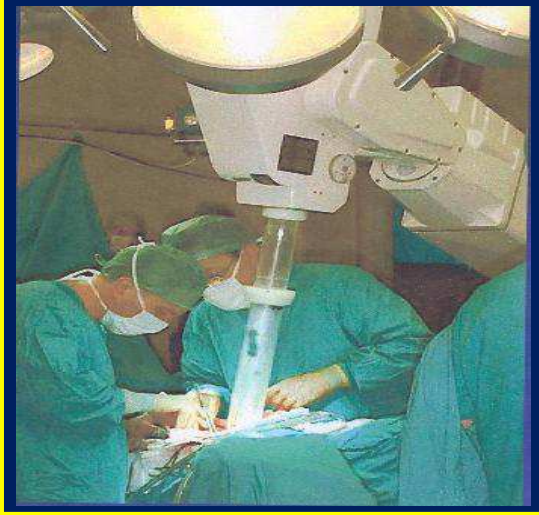


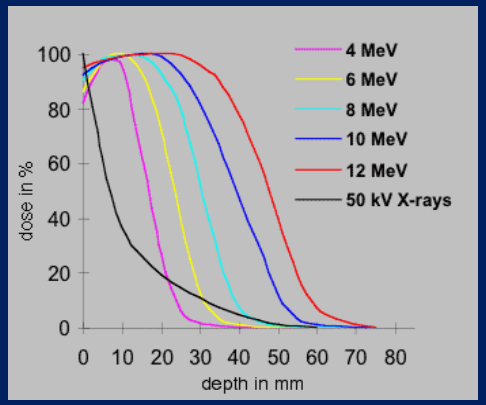

Part. Breast - Transversal
P
A
L
R
iso
bb
ref
Standard
Head First-Prone
Z: 5.37 cm
Z: 4.62 cm
Z: 3.87 cm
Z: 3.12 cm
Z: 2.37 cm
Z: 1.62 cm
Z: 0.87 cm
Z: 0.12 cm
Z: -0.63 cm

RADIOTERAPIA INTRAOPERATORIA

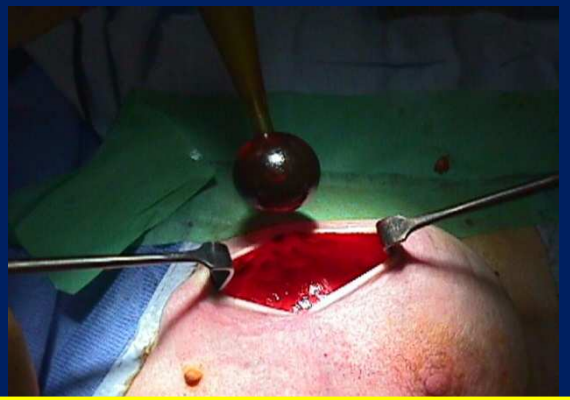
ELIOT



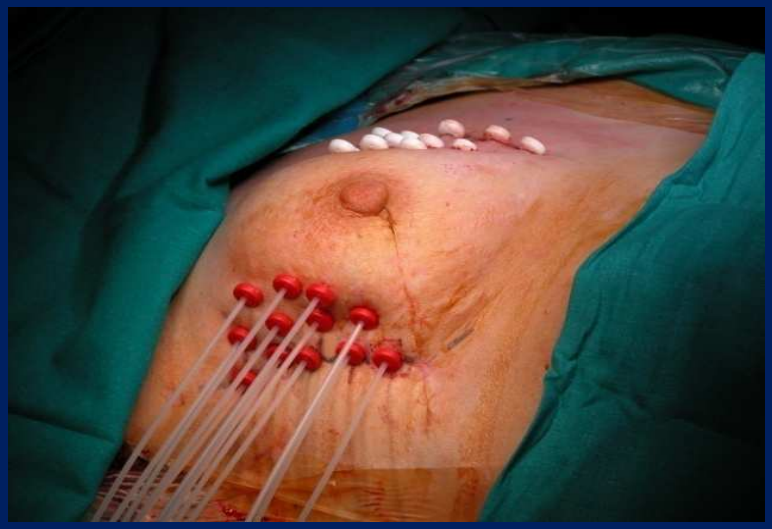




INTRABEAM



BRACHITERAPIA INTERSTIZIALE



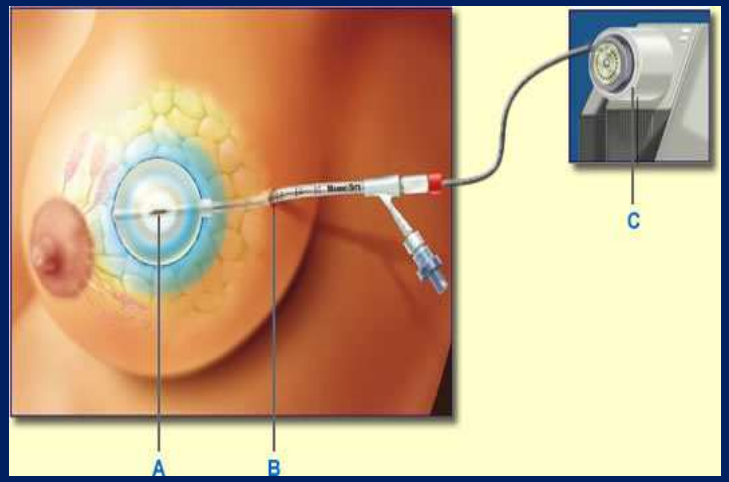
VANTAGGI

- Ottima conformazione della distribuzione di dose (anche per volumi bersaglio irregolari)
- Procedura riproducibile

SVANTAGGI

- Procedura abbastanza invasiva (può richiedere anestesia totale)
- Procedura operatore – dipendente (necessità di formazione del personale), time-consuming, complessa

MAMMOSITE



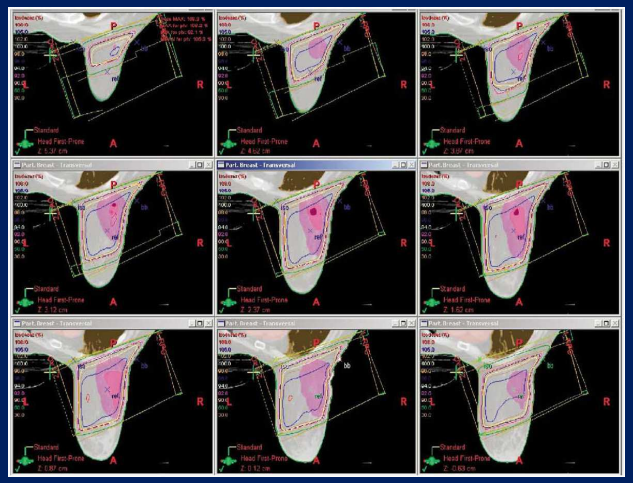
VANTAGGI

- Tecnica semplice, riproducibile e poco invasiva
- Piano di trattamento semplice

SVANTAGGI

- Difficile una buona conformazione della dose per volumi bersaglio non sferici
- Volume di irradiazione limitato (1 cm)

RTE 3D-CRT



VANTAGGI

- Tecnica non invasiva, ben accettata dalle pazienti
- Ottima distribuzione di dose

SVANTAGGI

- Piano di trattamento elaborato
- Tempi di trattamento lunghi (18-47 minuti)
- Imprecisione dovuta ai movimenti respiratori
- Maggior volume trattato

ELIOT

VANTAGGI

- Procedura, semplice, poco invasiva e bene accettata dalle pazienti
- Il radioterapista oncologo visualizza il letto tumorale, esposto durante l'intervento chirurgico.
- Tessuti ossigenati
- I tessuti sani circostanti sono protetti (schermi Al e Pb)

SVANTAGGI

- E' effettuata prima di conoscere l'esame istologico definitivo
- Rischio di tossicita' tardiva per l' impiego di una dose singola elevata

TARGIT: PRS 400 –INTRABEAM

VANTAGGI

- Piccole dimensioni dello strumento
- Utilizzo di raggi x di energie modeste → pochi problemi radioprotezionistici

SVANTAGGI

- Difficile una buona conformazione della dose per volumi bersaglio non sferici
- Utilizzo di raggi x di energie modeste→ rapida attenuazione della dose in profondita

  (20 Gy → 5 Gy a 1 cm)

confronto tra diversi frazionamenti in PBI

	α/β 2 Gy fibrosi	α/β 3 Gy	α/β 4 Gy teleangectasie	α/β 10 Gy
2 Gy → **50 Gy**	100	83	75	60
2 Gy → **60 Gy**	120	100	90	72
3.4 Gy → **34 Gy**	92	75	63	46
4 Gy → **32 Gy**	96	75	64	45
3.85 Gy → **38.5 Gy**	113	88	76	53
21 Gy	241	168	131	65
18Gy	180	126	99	50

PROBLEMATICHE APERTE E CONTROVERSIE

DOSI E FRAZIONAMENTO

confronto tra diversi frazionamenti in PBI - EQD2

	α/β 2 Gy fibrosi	α/β 3 Gy	α/β 4 Gy teleangectasie	α/β 10 Gy
2 Gy → 50 Gy	50	50	50	50
2 Gy → 60 Gy	60	60	60	60
3.4 Gy → 34 Gy	46	44	42	38
4 Gy → 32 Gy	48	45	43	37
3.85 Gy → 38.5 Gy	56	53	50	44
18 Gy	90	76	66	42
21 Gy	121	101	87	54

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Invasive Breast Cancer

NCCN Guidelines Index
Breast Cancer Table of Contents
Discussion

LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)

CLINICAL STAGE

Stage IIIA
T0, N2, M0
T1, N2, M0
T2, N2, M0
T3, N2, M0

Stage IIIA patients with T3, N1, M0 disease, see BINV-1

Stage IIIB
T4, N0, M0
T4, N1, M0
T4, N2, M0

Stage IIIC
Any T, N3, M0

Stage IV
Any T, any N, M1 → See Initial Workup for Stage IV Disease (BINV-16)

WORKUP

- History and physical exam
- CBC, platelets
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral mammogram, ultrasound as necessary
- Pathology review[a]
- Determination of tumor ER/PR status and HER2 status[b]
- Genetic counseling if patient is at high risk for hereditary breast cancer[c]
- Breast MRI[d] (optional), with special consideration for mammographically occult tumors
- Consider fertility counseling if indicated[e]

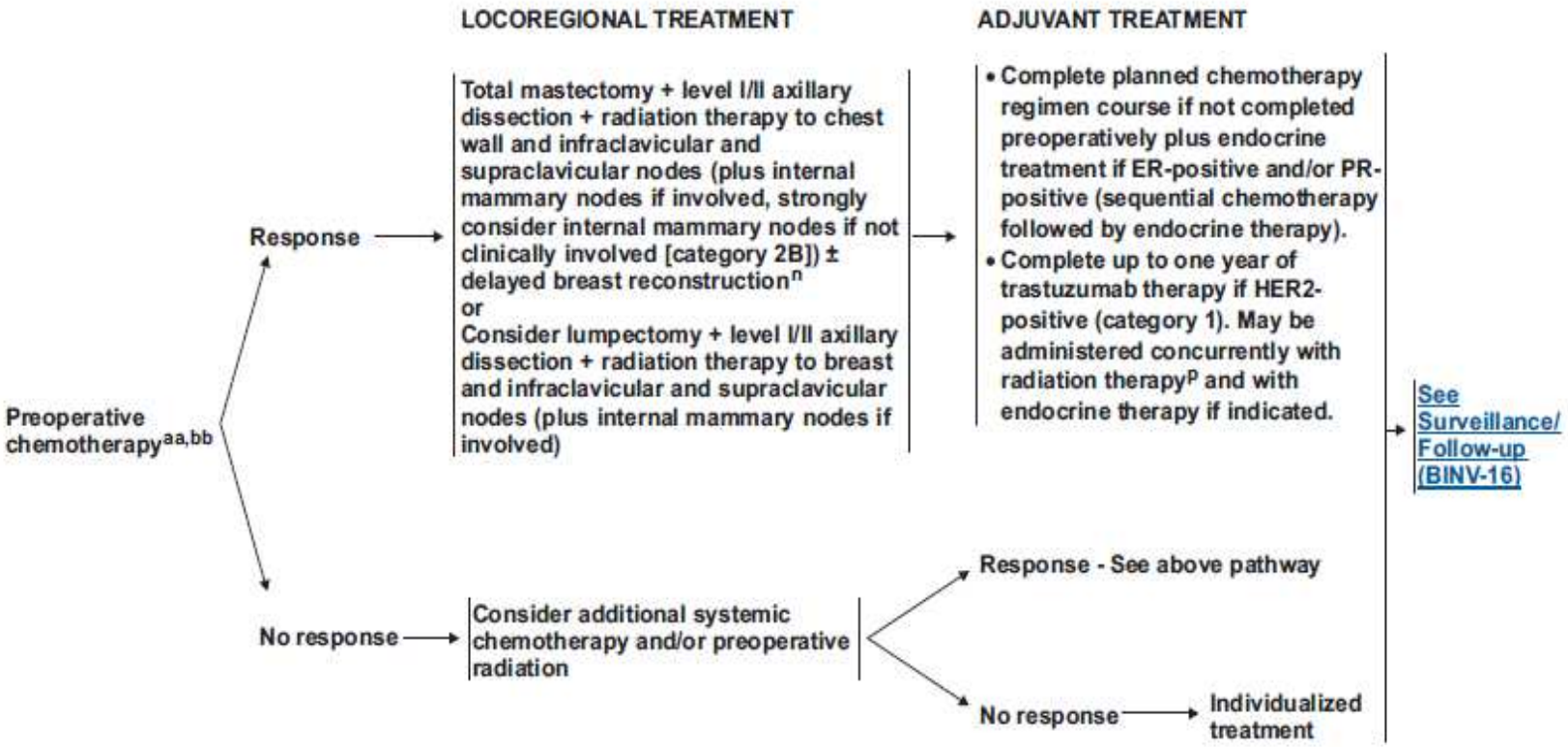
Consider systemic staging:
- Chest diagnostic CT
- Abdominal ± pelvic diagnostic CT or MRI
- Bone scan or sodium fluoride PET/CT[g] (category 2B)
- FDG PET/CT[h,i] (optional, category 2B)

Optional studies as directed by signs or symptoms:
- Bone scan indicated if localized bone pain or elevated alkaline phosphatase
- Abdominal ± pelvic diagnostic CT or MRI indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis
- Chest diagnostic CT if pulmonary symptoms present

→ See Preoperative Chemotherapy (BINV-15)

[a] The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and noninvasive carcinomas of the breast. http://www.cap.org.
[b] See Principles of HER2 Testing (BINV-A).
[c] See NCCN Guidelines for Genetics/Familial High-Risk Assessment: Breast and Ovarian.
[d] See Principles of Dedicated Breast MRI Testing (BINV-B).
[e] See Fertility and Birth Control After Adjuvant Breast Cancer Treatment (BINV-C).
[g] If FDG PET/CT is performed and clearly indicates bone metastasis, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.
[h] FDG PET/CT can be performed at the same time as diagnostic CT. The use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.
[i] FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.

PREOPERATIVE CHEMOTHERAPY FOR LOCALLY ADVANCED INVASIVE BREAST CANCER (NON-INFLAMMATORY)



[n] See Principles of Breast Reconstruction Following Surgery (BINV-H).

[p] See Principles of Radiation Therapy (BINV-I).

[aa] Anumber of combination and single-agent chemotherapy regimens have activity in the preoperative setting. Those chemotherapy regimens recommended in the adjuvant setting (See BINV-K) may be considered in the preoperative setting. If treated with endocrine therapy, an aromatase inhibitor is preferred for postmenopausal women.

[bb] Patients with HER2-positive tumors should be treated with preoperative chemotherapy incorporating trastuzumab for at least 9 weeks of preoperative therapy (See BINV-K).

TOSSICITA’

SURVEILLANCE/FOLLOW-UP

- History and physical exam every 4-6 mo for 5 y, then every 12 mo
- Annual mammography
- Women on tamoxifen: annual gynecologic assessment every 12 mo if uterus present
- Women on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter[99]
- Assess and encourage adherence to adjuvant endocrine therapy
- Evidence suggests that active lifestyle and achieving and maintaining an ideal body weight (20-25 BMI) may lead to optimal breast cancer outcomes

→ See Recurrent Disease (BINV-17)

[99] The use of estrogen, progesterone, or selective estrogen receptor modulators to treat osteoporosis or osteopenia in women with breast cancer is discouraged. The use of a bisphosphonate is generally the preferred intervention to improve bone mineral density. Optimal duration of bisphosphonate therapy has not been established. Factors to consider for duration of anti-osteoporosis therapy include bone mineral density, response to therapy, and risk factors for continued bone loss or fracture. Women treated with a bisphosphonate should undergo a dental examination with preventive dentistry prior to the initiation of therapy, and should take supplemental calcium and vitamin D.