



Gruppo Regionale  
AIRO APPULO-LUCANO

## La Radioterapia nel cancro della mammella: indicazioni e tecnica

Il Convegno  
del Gruppo Regionale AIRO APPULO-LUCANO

**Taranto, 19 giugno 2010**

Auditorium Ospedale SS. Annunziata  
Padiglione Vinci

Il trattamento dei drenaggi linfonodali  
**G. Lazzari**

# STATO DELL'ARTE



**accordo tra radioterapisti**



**studi randomizzati in corso**

# EVIDENCE BASED MEDICINE

## Locoregional Radiation Therapy in High-Risk Breast Cancer: 20-Year Results of the PRBS Trial

Joseph Ragaz, Ivo A. Olivetto, Jon...

## Does Locoregional Radiation Therapy Improve Survival in Breast Cancer? A Meta-Analysis

Whelan, Jim Julian, Jim Wright, Alejandro R. Jaccad, and Mark L. Levine

ELSEVIER  
doi:10.1016/j.ijrobp.2010.03.001  
CLINICAL INVESTIGATION  
OUTCOME AFTER CONSERVATIVE SURGERY AND BREAST IRRADIATION IN 5,717 PATIENTS WITH BREAST CANCER: IMPLICATIONS FOR SUPRACLAVICULAR NODAL IRRADIATION  
LORENZO LIVI, M.D., \* VIERI SCOTTI, M.D., \* CALOGERO SAIEVA, M.D., † ICRO MEATTINI, M.D., \* BEATRICE DETTI, M.D., \* GABRIELE SIMONTACCHI, M.D., \* CARLA DELUCA CARDILLO, M.D., \* FABIOLA PALAR, M.D., \* MONICA MANGIONI, M.D., \* LIVIA MARRAZZO, Ph.D., † BENEDETTA AGRESTI, M.D., \* LUIGI CATALIOTTI, M.D., § SIMONETTA BIANCHI, M.D., || AND GIAMPAOLO BITI, M.D., \*

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0958-2017(2010)031-0001-0

Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)\*

...omy irradiation limited to positive nodes, as recommended reports? A subgroup analysis of the 16 randomized trials<sup>☆</sup>

, Hanne M. Nielsen<sup>a,b</sup>, Jens Overgaard<sup>b</sup>

# RT DRENAGGI IN BCS

- In corso l'analisi di due studi randomizzati

## **EORTC trial 22922-10925**

*tumori mediali N+ - random RT su svc  
mediale e CMI vs no LN RT*

## **MA -20**

*tumori N+ o N0 alto rischio- random RT su  
svc, apice ascella, CMI vs no LN RT*

# RT DRENAGGI SU MASTECTOMIA

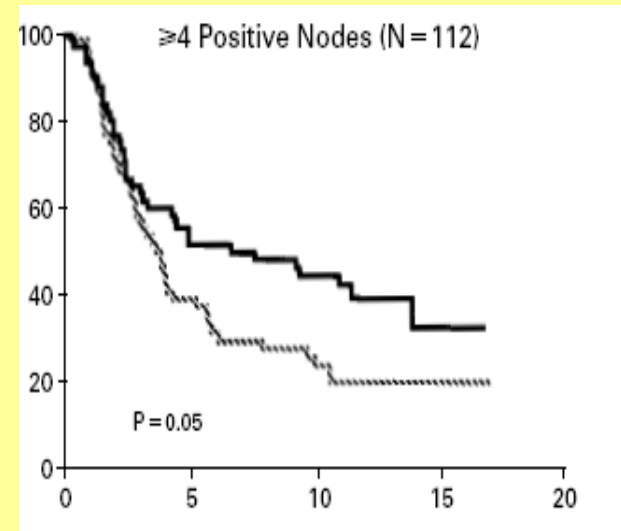
The New England Journal of Medicine **1997**

## ADJUVANT RADIOTHERAPY AND CHEMOTHERAPY IN NODE-POSITIVE PREMENOPAUSAL WOMEN WITH BREAST CANCER

JOSEPH RAGAZ, STEWART M. JACKSON, NHU LE, IAN H. PLENDERLEITH, JOHN J. SPINELLI, VIVIAN E. BASCO,  
KENNETH S. WILSON, MARGARET A. KNOWLING, CHRISTOPHER M.L. COPPIN, MARILYN PARADIS, ANDREW J. GOLDMAN,  
AND IVO A. OLIVOTTO

## Locoregional Radiation Therapy in Patients With High- Risk Breast Cancer Receiving Adjuvant Chemotherapy: 20-Year Results of the British Columbia Randomized Trial

*Joseph Ragaz, Ivo A. Olivotto, John J. Spinelli, Norman Phillips, Stewart M.*  
Journal of the National Cancer Institute, Vol. 97, No. 2, January 19, 2005



**Canada**

# RT DRENAGGI SU MASTECTOMIA

## The New England Journal of Medicine

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VOLUME 337

OCTOBER 2, 1997

NUMBER 14



POSTOPERATIVE RADIOTHERAPY IN HIGH-RISK PREMENOPAUSAL WOMEN  
WITH BREAST CANCER WHO RECEIVE ADJUVANT CHEMOTHERAPY

MARIE OVERGAARD, M.D., PER S. HANSEN, M.D., JENS OVERGAARD, M.D., CARSTEN ROSE, M.D.,  
MICHAEL ANDERSSON, M.D., FLEMMING BACH, M.D., MOGENS KJAER, M.D., CARL C. GADEBERG, M.D.,  
HENNING T. MOURIDSEN, M.D., MAJ-BRITT JENSEN, M.Sc., AND KARIN ZEDELER, M.Sc.,  
FOR THE DANISH BREAST CANCER COOPERATIVE GROUP 82b TRIAL

*Lancet* 2005; 366: 2087-2106

Effects of radiotherapy and of differences in the extent of  
surgery for early breast cancer on local recurrence and  
15-year survival: an overview of the randomised trials



Early Breast Cancer Trialists' Collaborative Group (EBCTCG)\*

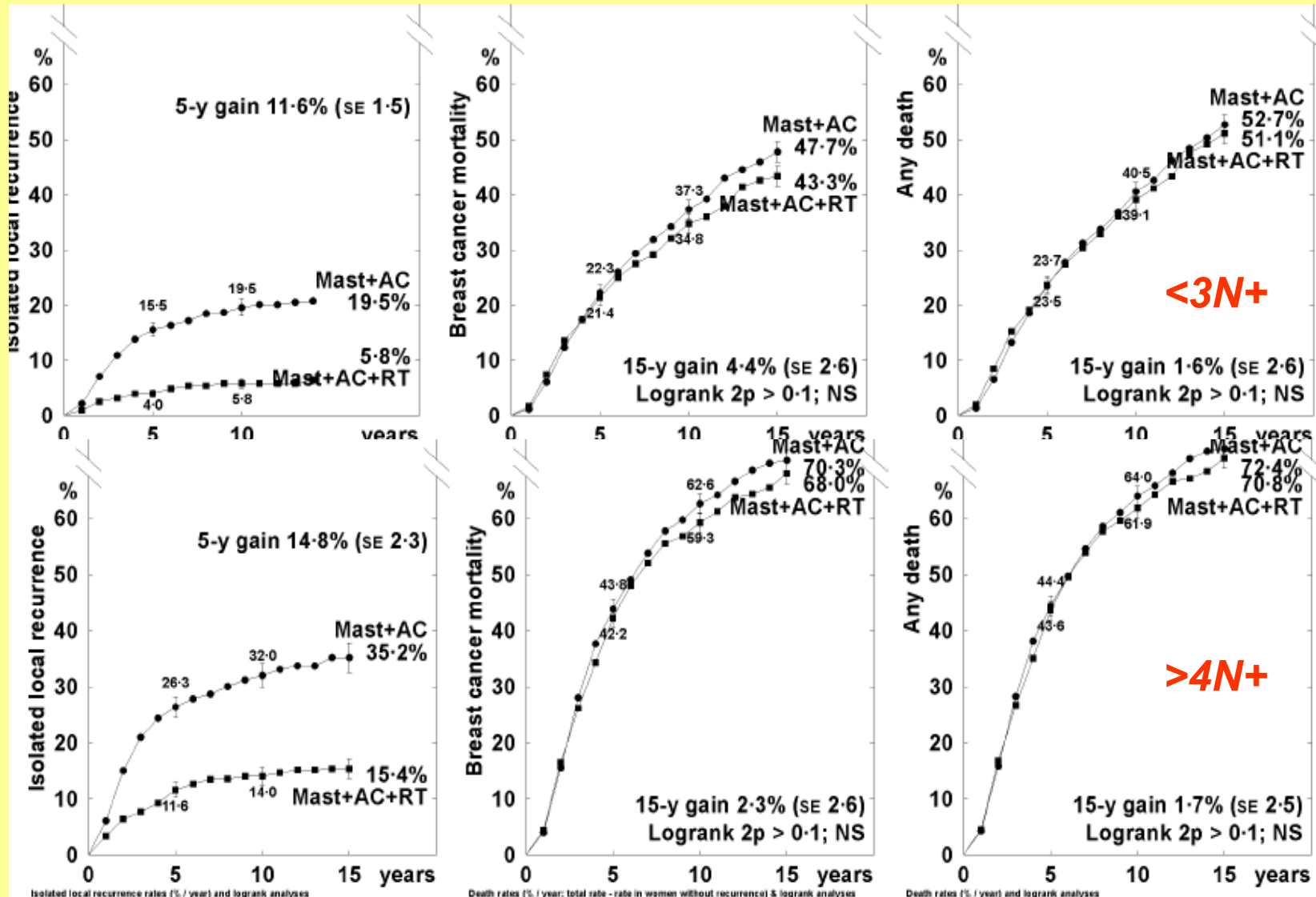
**TABLE 4. COX MULTIVARIATE PROPORTIONAL-HAZARDS ANALYSIS OF THE RELATIVE RISK OF ANY TYPE OF RECURRENCE OR DEATH OR OF DEATH FROM ANY CAUSE. \***

| VARIABLE   | ANY TYPE OF RECURRENCE<br>OR DEATH |                  | DEATH      |                  |
|--|------------------------------------|------------------|------------|------------------|
|  | P<br>VALUE                         | RR<br>(95% CI)   | P<br>VALUE | RR<br>(95% CI)   |
| Tumor size (<21 mm, 21-50 mm,<br>>50 mm)†            | <0.001                             | 1.43 (1.30-1.58) | <0.001     | 1.49 (1.35-1.65) |
| No. of positive nodes (0, 1-3, >3)†                  | <0.001                             | 1.57 (1.36-1.81) | <0.001     | 1.75 (1.50-2.05) |
| Frequency of positive nodes (<34%,<br>34-67%, >67%)† | <0.001                             | 1.44 (1.30-1.58) | <0.001     | 1.38 (1.24-1.53) |
| Grade of anaplasia (I, II, III)†                     | <0.001                             | 1.44 (1.31-1.59) | <0.001     | 1.52 (1.37-1.70) |
| Age of 40 to 49 yr (vs. <40 yr and<br>50-59 yr)      | <0.001                             | 0.73 (0.64-0.83) | <0.001     | 0.76 (0.66-0.87) |
| Radiotherapy + CMF (vs. CMF alone)                   | <0.001                             | 0.59 (0.51-0.67) | <0.001     | 0.71 (0.62-0.82) |

Europa

# MASTECTOMIA RT & N+

metanalisi Lancet 2005



## **Postmastectomy Radiotherapy: Guidelines of the American Society of Clinical Oncology**

By Abram Recht, Stephen B. Edge, Lawrence J. Solin, David S. Robinson, Alison Estabrook, Richard E. Fine, Gini F. Fleming, Silvia Formenti, Clifford Hudis, Jeffrey J. Kirshner, David A. Krause, Robert R. Kuske, Amy S. Langer, George W. Sledge, Jr, Timothy J. Whelan, and David G. Pfister for the American Society of Clinical Oncology

### 8. Axillary Nodal Irradiation

We suggest that full axillary radiotherapy not be given routinely to patients undergoing complete or level I/II axillary dissection. There is insufficient evidence to make suggestions or recommendations as to whether some patient subgroups might benefit from axillary irradiation.

### 9. Supraclavicular Nodal Irradiation for Patients With Four or More Positive Axillary Lymph Nodes

The incidence of clinical supraclavicular failure is sufficiently great in patients with four or more positive axillary nodes that we suggest a supraclavicular field should be irradiated in all such patients.

### 10. Supraclavicular Nodal Irradiation for Patients With One to Three Positive Axillary Lymph Nodes

???

There is insufficient evidence to state whether a supraclavicular field should or should not be used for patients with one to three positive axillary nodes.

### 11. Internal Mammary Nodal Irradiation

There is insufficient evidence to make suggestions or recommendations on whether deliberate internal mammary nodal irradiation should or should not be used in any patient subgroup.

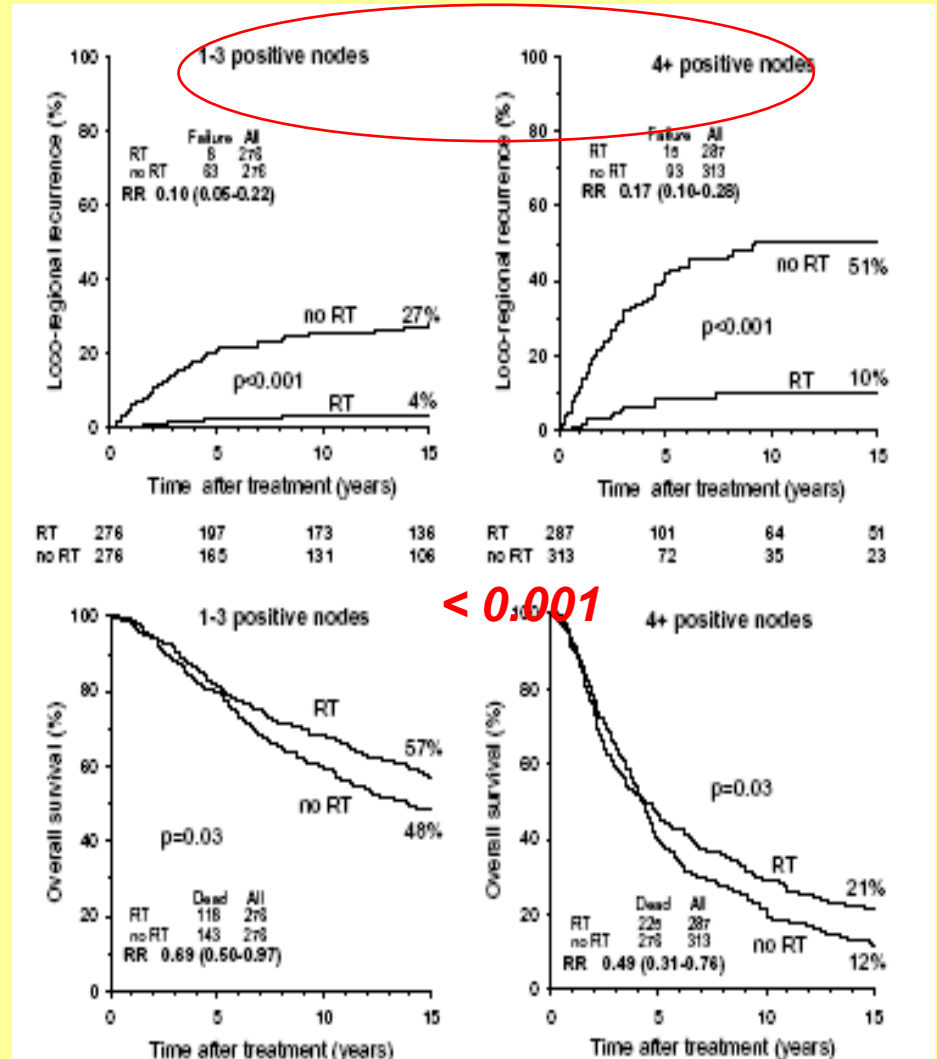


# EVIDENZE PZ $N+ < 3$

Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c randomized trials<sup>☆</sup>

**R&O 2007**

Marie Overgaard<sup>a,\*</sup>, Hanne M. Nielsen<sup>a,b</sup>, Jens Overgaard<sup>b</sup>



# FATTORI DI RISCHIO PZ $N+ < 3$

- ***Nodal ratio***
- ***Età 50 aa Grading, LVI, status recettoriale***
- ***Estensione extracapsulare***
- ***Metastasi linfonodale  $\geq 2$  cm***
- ***Entità della dissezione ascellare***

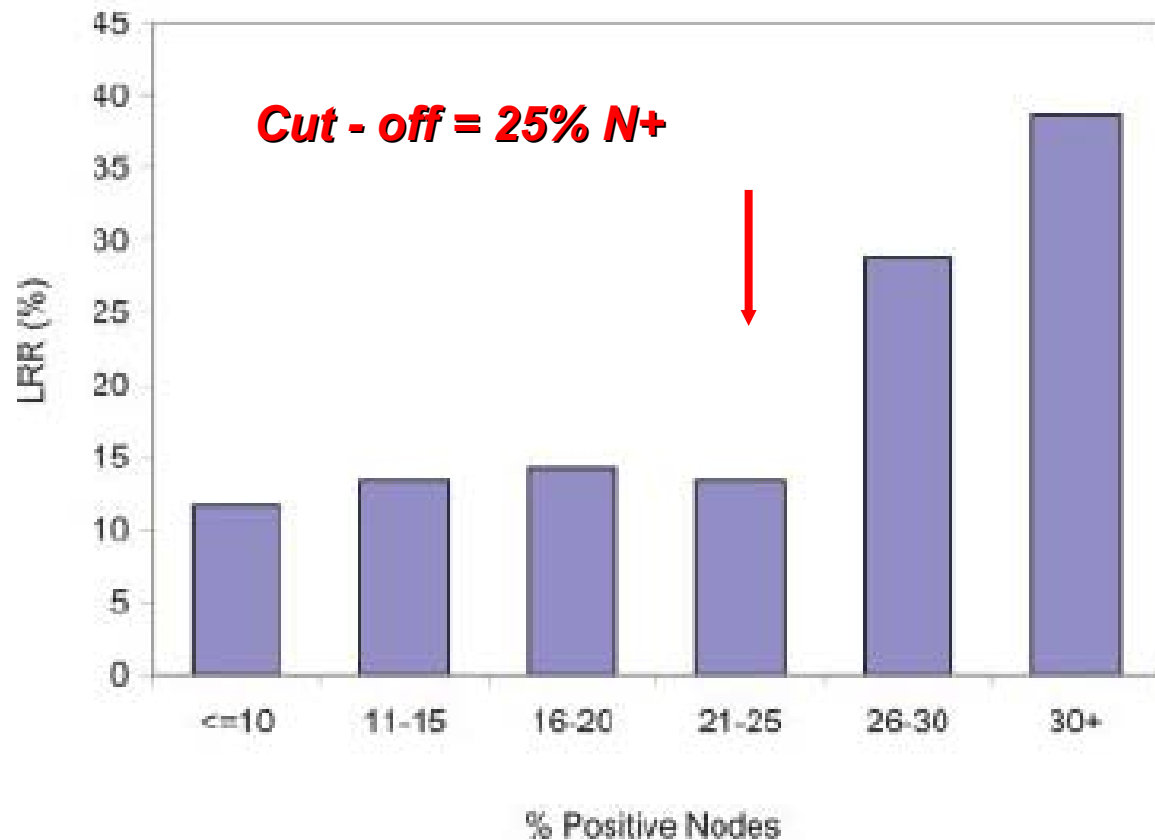
# The Prognostic Significance of the Percentage of Positive/Dissected Axillary Lymph Nodes in Breast Cancer Recurrence and Survival in Patients with One to Three Positive Axillary Lymph Nodes *Cancer, 2005*

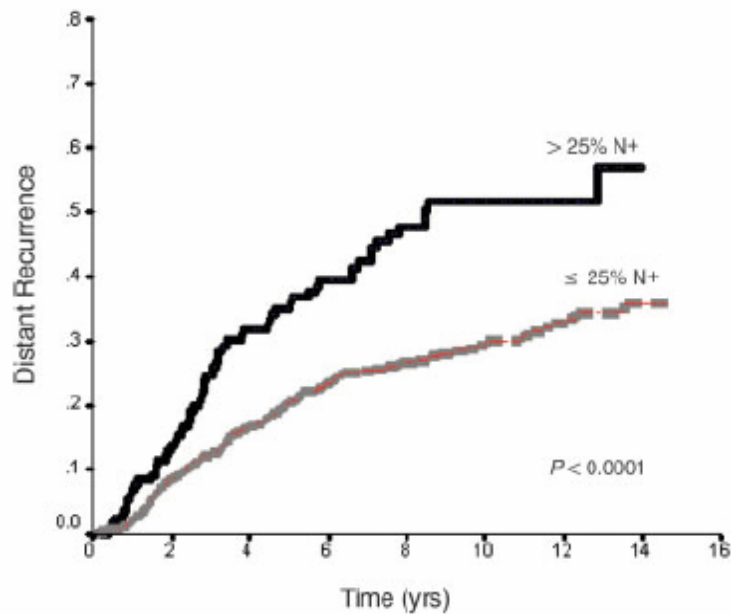
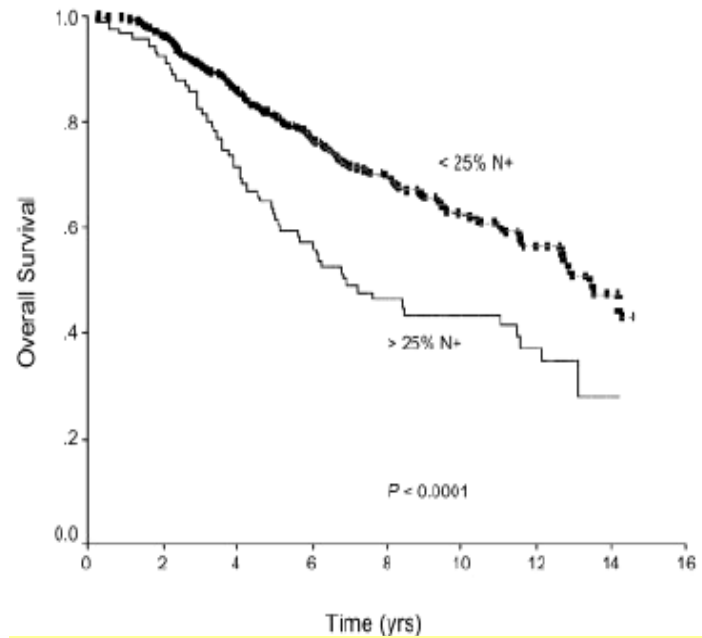
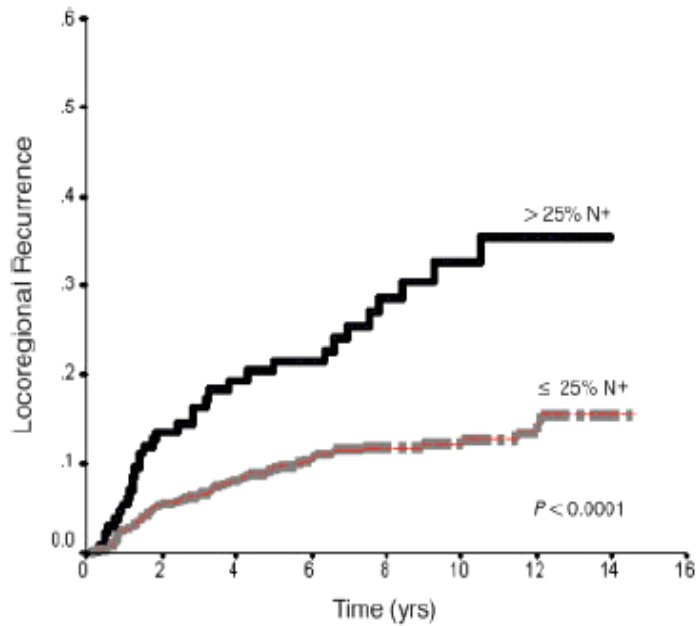
Pauline T. Truong, M.D.<sup>1,2</sup>  
Eric Berthelet, M.D.<sup>1</sup>

**LRR 10aa**

**13.9%  $N + \leq 25\%$**

**36.7%  $N + > 25\%$**



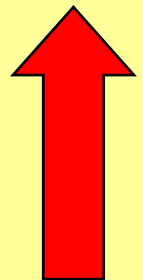


**$N+ > 25\%$  :**  **$P < 0.001$**

**Recidiva locale**

**OS** ↓

**Malattia a distanza**



**Truong, Cancer, 2005**

## CLINICAL INVESTIGATION

THE RATIO OF POSITIVE TO EXCISED NODES IDENTIFIES HIGH-RISK SUBSETS AND REDUCES INTER-INSTITUTIONAL DIFFERENCES IN LOCOREGIONAL RECURRENCE RISK ESTIMATES IN BREAST CANCER PATIENTS WITH 1-3 POSITIVE NODES: AN ANALYSIS OF PROSPECTIVE DATA FROM BRITISH COLUMBIA AND THE M. D. ANDERSON CANCER CENTER

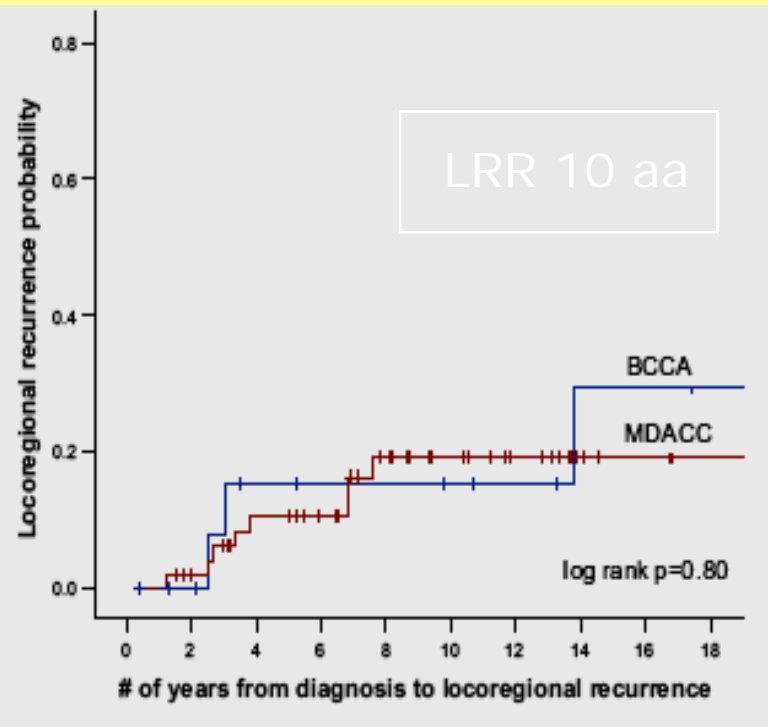
*Int J Radiat Onc Biol Phys, 2007*

PAULINE T. TRUONG, M.D., C.M.,\*† WENDY A. WOODWARD, M.D., PH.D.,‡

***Nodal Ratio***  
**0.20-0.29**

**BCCA 28.7%**

**MDACC 22.7%**



PATIENTS WITH T1 TO T2 BREAST CANCER WITH ONE TO THREE POSITIVE NODES HAVE HIGHER LOCAL AND REGIONAL RECURRENCE RISKS COMPARED WITH NODE-NEGATIVE PATIENTS AFTER BREAST-CONSERVING SURGERY AND WHOLE-BREAST RADIOTHERAPY

*pT1- pT2 pN1 vs pN0*

PAULINE T. TRUONG, M.D., C.M., F.R.C.P.C.,\*† STUART O. JONES, B.Sc.,\* HOSAM A. KADER, M.D.,

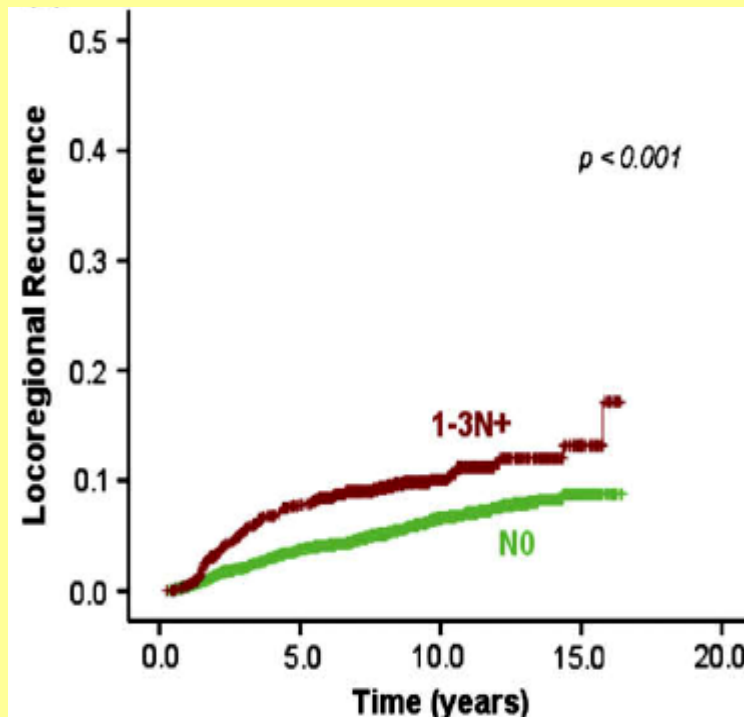
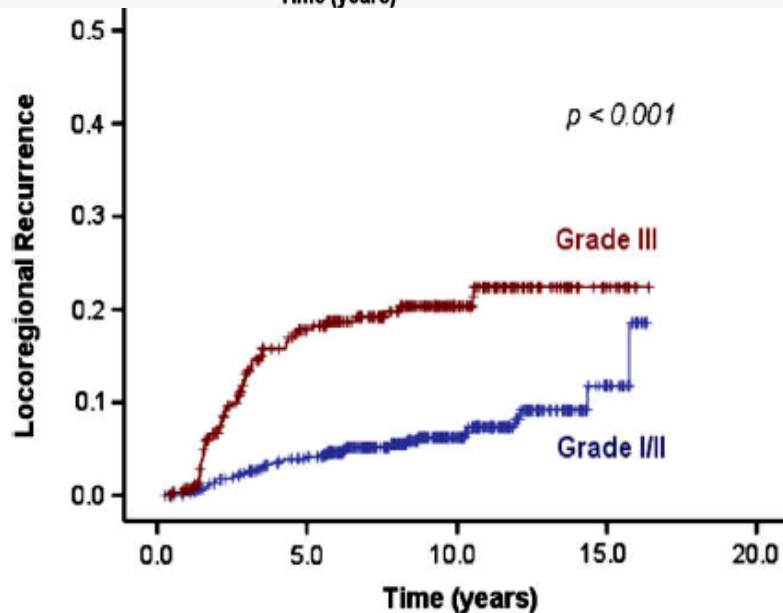
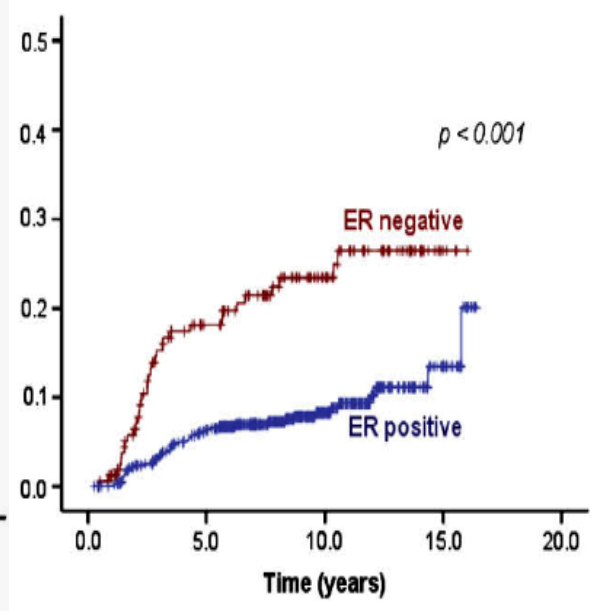
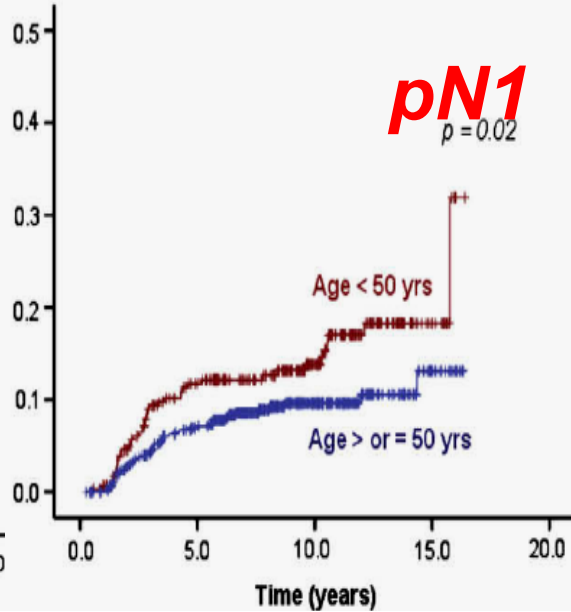
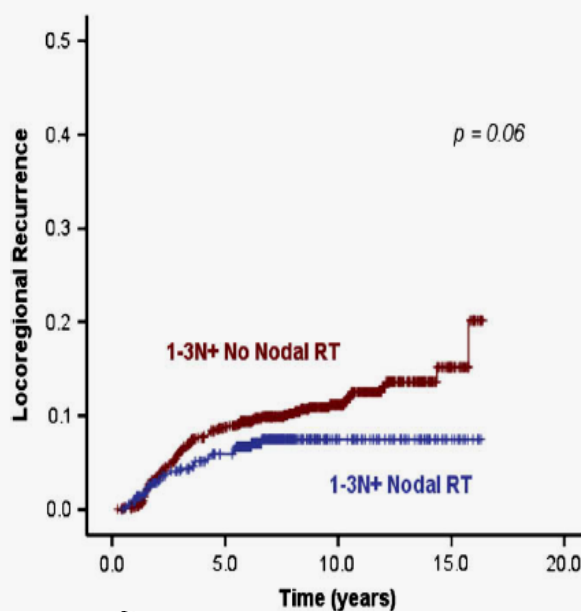


Table 3. Sites of regional recurrence in patients with node-negative (N0) and one-to-three nodes positive (1-3N+) breast cancer

| Regional recurrence          | Entire cohort (n = 5,688) | N0 (n = 4,433) | 1-3N+ (n = 1,255) |
|------------------------------|---------------------------|----------------|-------------------|
| Total                        | 155 (2.7)                 | 87 (2.0)       | 68 (5.4)          |
| Axillary nodes               | 90 (1.6)                  | 50 (1.1)       | 40 (3.2)          |
| Supra-/infraclavicular nodes | 59 (1.0)                  | 32 (0.7)       | 27 (2.2)          |
| Internal mammary nodes       | 5 (0.1)                   | 4 (0.1)        | 1 (0.1)           |
| >1 Regional nodal site       | 1 (0.02)                  | 1 (0.02)       | 0 (0)             |



| Variable                           | Hazard ratio (95% confidence interval) | p      |
|------------------------------------|--|--------|
| Age (y) (<50 vs. ≥50)              | 1.58 (1.25–2.0)                        | <0.001 |
| Histology (lobular vs. ductal)     | 0.83 (0.45–1.52)                       | 0.54   |
| T stage (T2 vs. T1)                | 1.31 (1.00–1.70)                       | 0.05   |
| Nodal status (1–3N+ vs. N0)        | 1.85 (1.34–2.55)                       | <0.001 |
| % Positive nodes (>20% vs. ≤20%)   | 1.64 (1.01–2.49)                       | 0.02   |
| Grade (III vs. I/II)               | 1.96 (1.51–2.53)                       | <0.001 |
| LVI status (positive vs. negative) | 1.54 (1.17–2.02)                       | 0.002  |
| ER status (negative vs. positive)  | 1.29 (0.99–1.69)                       | 0.06   |
| Nodal RT (yes vs. no)              | 0.59 (0.38–0.92)                       | 0.02   |
| Systemic therapy (yes vs. no)      | 0.59 (0.44–0.80)                       | 0.001  |

Locoregional recurrence

**EXTRACAPSULAR AXILLARY NODE EXTENSION IN PATIENTS RECEIVING ADJUVANT SYSTEMIC THERAPY: AN INDICATION FOR RADIOTHERAPY?**

B. J. FISHER, M.D.,\* F. E. PERERA, M.D.,\* A. L. COOKE, M.D.,† A. OPEITUM, M.D.,‡

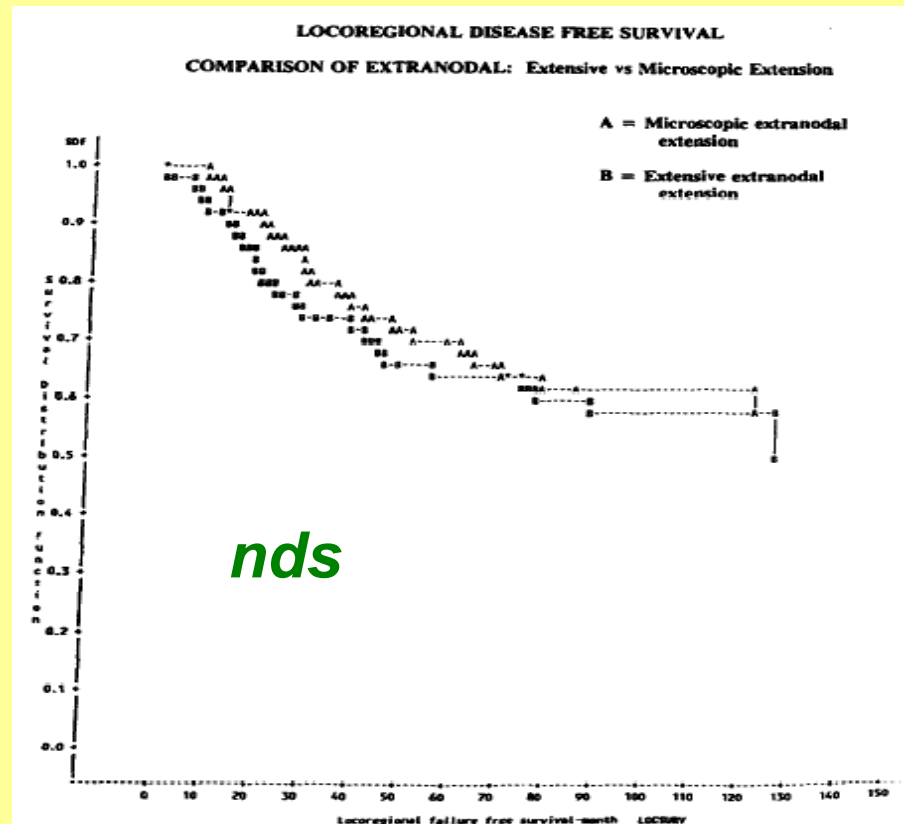
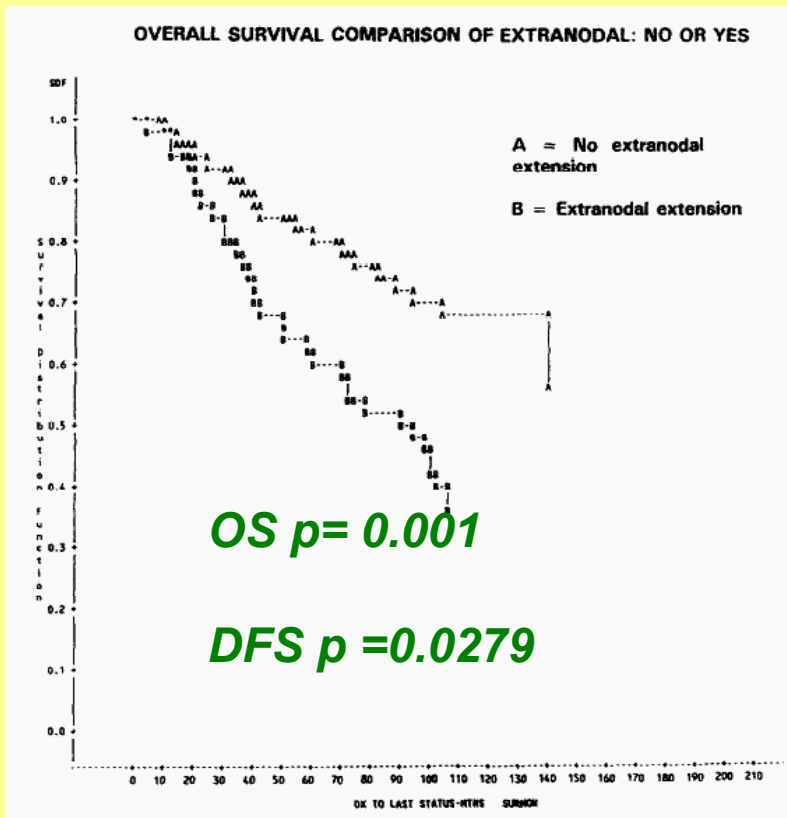




Table 2. Sites of recurrence by extranodal extension in patients who received chemotherapy/tamoxifen only

| Site                            | Extranodal extension<br>n = 64/82 | No extranodal extension<br>n = 52/172 |
|---------------------------------|-----------------------------------|---------------------------------------|
| <b>Local</b>                    |                                   |                                       |
| Total                           | 17/82 (21%)                       | 17/172 (10%)                          |
| Breast                          | 9/25 (36%)                        | 9/51 (18%)                            |
| Chest wall                      | 8/57 (14%)                        | 8/120 (7%)                            |
| <b>Regional</b>                 |                                   |                                       |
| Total                           | 17/82 (21%)                       | 18/172 (11%)                          |
| Axilla                          | 6/82 (7%)                         | 6/172 (4%)                            |
| Supraclavicular nodes           | 10/82 (12%)                       | 10/172 (6%)                           |
| Internal mammary nodes          | 1/82 (1%)                         | 1/172 (<1%)                           |
| Multiple                        | 0                                 | 1/172 (<1%)                           |
| <b>Locoregional</b>             |                                   |                                       |
| Distant metastases              | 2/82 (2%)                         | 2/172 (1%)                            |
| <b>Locoregional and distant</b> |                                   |                                       |
| No recurrence                   | 18/82 (22%)                       | 120/172 (70%)                         |

Table 3. Patterns of first recurrence based upon extranodal extension and number of positive axillary nodes

| Experienced cal recurrence   | Extra nodal extension (n = 82) |           | No extra nodal extension (n = 172) |           |
|--|--------------------------------|-----------|------------------------------------|-----------|
|  | 1-3 Nodes                      | ≥4 Nodes  | 1-3 Nodes                          | ≥4 Nodes  |
| Local first recurrence by extra nodal extension and # positive axillary nodes    |                                |           |                                    |           |
| Yes  | 9 (23.7%)                      | 8 (19.5%) | 18 (16.1%)                         | 9 (15.0%) |
| No   | 29                             | 33        | 94                                 | 51        |
| Regional first recurrence by extra nodal extension and # positive axillary nodes |                                |           |                                    |           |
| Yes  | 9 (23.7%)                      | 6 (14.6%) | 15 (13.4%)                         | 8 (13.3%) |
| No   | 29                             | 35        | 97                                 | 52        |
| Distant first recurrence by extra nodal extension and # positive axillary nodes  |                                |           |                                    |           |
| Yes  | 9 (23.7%)                      | 6 (14.6%) | 15 (13.4%)                         | 8 (13.3%) |
| No   | 29                             | 35        | 97                                 | 52        |

Table 6. Univariate analysis of prognostic factors for actuarial survival within the extranodal extension group

| Factor   | Log rank | Wilcoxon |
|--|----------|----------|
| Type of mastectomy                                     | 0.5836   | 0.9194   |
| Age  | 0.3392   | 0.2190   |
| Tumor size   | 0.5187   | 0.5705   |
| # Positive axillary nodes                              | 0.0137   | 0.0045   |
| Extent extracapsular Extension (gross vs. microscopic) | 0.922    | 0.9848   |
| % Ideal dose   | 0.2871   | 0.4306   |
| % Ideal dose intensity                                 | 0.4727   | 0.688    |
| ER negative  | 0.0100   | 0.0003   |
| PR negative  | 0.0217   | 0.0029   |
| ER and PR negative                                     | 0.0039   | 0.0001   |

# ECE

- **fattore prognostico avverso** *(non indipendente)*  
**x sopravvivenza e recidiva locale**
- **In ECE + lo status ER-/PR e N +> 4 sono fattori avversi x la sopravvivenza**
- **ECE + raddioppia % di recidiva su mammella, parete e sovraclaveare indipendentemente dal N + ascellari**

# QUALI PZ N+ < 3 alto rischio ?

- **448 pz N+< 3 no RT su sovraclaveare**
- **N mediano di 17 lns escissi ( 5-53)**
- **CT nel 99% pz**
- **144 pz con RT adiuvante**
- **recidiva 101 pz ( 22.5%) in cui 8.7% svc**

DETERMINING WHICH PATIENTS REQUIRE IRRADIATION OF THE SUPRACLAVICULAR NODAL AREA AFTER SURGERY FOR N1 BREAST CANCER

JEONG IL YU, M.D.,\* WON PARK, M.D., PH.D.,\* SEUNG JAE HUH, M.D., PH.D.,\* DOO HO CHOI, M.D.,

Table 3. Prognostic factors of SCRFS rate

| Variable                      | 5-y SCRFS rate (%) | p Value    |              |
|-------------------------------|--------------------|------------|--------------|
|                               |                    | Univariate | Multivariate |
| Age                           |                    | 0.6367     | 0.2811       |
| <35 y                         | 92.6               |            |              |
| ≥35 y                         | 94.2               |            |              |
| Location                      |                    | 0.0060     | 0.1748       |
| Inner                         | 84.3               |            |              |
| Other                         | 94.7               |            |              |
| Histology                     |                    | 0.9191     | 0.4947       |
| Invasive ductal               | 92.5               |            |              |
| Other                         | 92.8               |            |              |
| Pathologic T stage            |                    | 0.0019     | 0.0975       |
| 1-2                           | 93.3               |            |              |
| 3                             | 63.3               |            |              |
| Grade                         |                    | 0.7291     | 0.8259       |
| 1-2                           | 93.3               |            |              |
| 3                             | 92.0               |            |              |
| Hormone receptor              |                    | 0.8414     | 0.6182       |
| Positive                      | 92.9               |            |              |
| Negative                      | 92.6               |            |              |
| Lymphovascular invasion       |                    | <0.0001    | <0.0001      |
| Positive                      | 83.0               |            |              |
| Negative                      | 94.8               |            |              |
| No. of positive ALN           |                    | <0.0001    | 0.0003       |
| 1                             | 98.3               |            |              |
| 2-3                           | 86.3               |            |              |
| Highest level of positive ALN |                    | <0.0001    | 0.0120       |
| I                             | 93.8               |            |              |
| II-III                        | 74.7               |            |              |
| Percentage of positive ALN    |                    | <0.0001    | 0.0509       |
| ≤20%                          | 95.4               |            |              |
| >20%                          | 82.1               |            |              |
| Extracapsular extension       |                    | <0.0001    | <0.0001      |
| Positive                      | 54.6               |            |              |
| Negative                      | 94.6               |            |              |

invasione linfovaskolare

p < 0.001

ECE

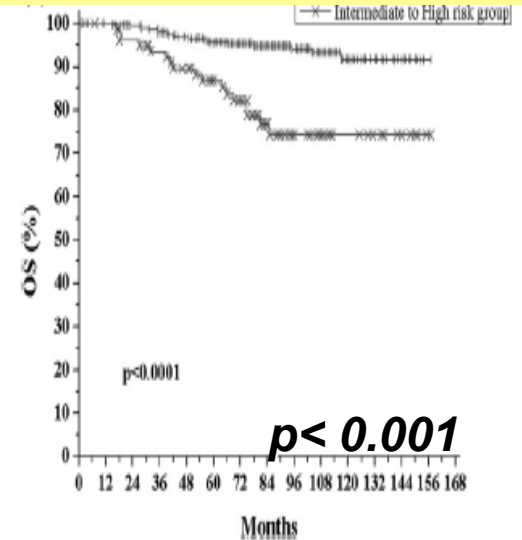
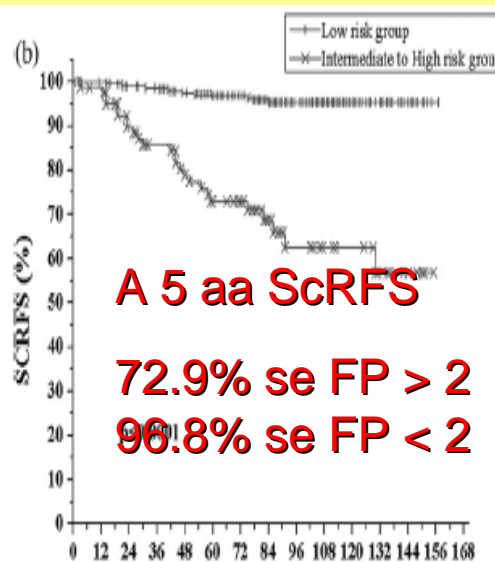
p < 0.0001

numero lns positivi

p = 0.0003

livello dei lns positivi

p = 0.012



# RT SOVRACLAVEARE

- Si raccomanda nelle pazienti  $N+ > 4$  lns
- Evidenze in pazienti  $N + < 3$  lns

da considerare se



- ✓ ***ECE***
- ✓ ***Nodal ratio > 25%***
- ✓ ***Età premenopausa***
- ✓ ***ER / PR negativi***
- ✓ ***Invasione linfovaskolare***

***FP > 2***

# RT ASCELLA

- **Non è giustificata se dissezione ascellare adeguata ( 7-10 lns) ed indagati i livelli I-II indipendentemente dallo stato N+** *(ASCO 2000, EUSOMA Working Party 2002)*
- **E' giustificata in assenza di clearance ascellare o se vi è residuo di malattia**
- **Da valutare dopo LNs +** *(Galper, IJROBP,2000)*
- **RT in ascella N+ è efficace quanto la chirurgia - linfedema ?-**

*( Veronesi,Annals of Oncology 2005)*

RISK FACTORS FOR REGIONAL NODAL FAILURE AFTER BREAST-  
CONSERVING THERAPY: REGIONAL NODAL IRRADIATION REDUCES  
RATE OF AXILLARY FAILURE IN PATIENTS WITH FOUR OR MORE  
POSITIVE LYMPH NODES

INGA S. GRILLS, M.D.,\* LARRY L. KESTIN, M.D.,\* NEAL GOLDSTEIN, M.D.,†

## Sopravvivenza attuariale a 10 y pz N+

- **< 6** Ins escissi = **33%**
- **6-10** Ins escissi = **63%**
- **> 10** Ins escissi = **65%**

***p = 0.05***

**SHOULD INTERNAL MAMMARY LYMPH NODES IN BREAST CANCER BE A TARGET FOR THE RADIATION ONCOLOGIST?**

GARY M. FREEDMAN, MD,\* BARBARA L. FOWBLE, MD,\* NICOS NICOLAOU, MD,\*  
ELIN R. SIGURDSON, MD,† MICHAEL H. TOROSIAN, MD,† MARCIA C. BORAAS, MD,† AND  
JOHN P. HOFFMAN, MD†

\*Department of Radiation Oncology, and †Department of Surgical Oncology, Fox Chase Cancer Center, Philadelphia PA

Table 1. Incidence of positive internal mammary lymph nodes in operable breast cancer by axillary node status and primary tumor location

| Series                      | #    | IMN positive (%) |         |       |       |                 |         |       |       |
|-----------------------------|------|------------------|---------|-------|-------|-----------------|---------|-------|-------|
|                             |      | Axilla negative  |         |       |       | Axilla positive |         |       |       |
|                             |      | Inner            | Central | Outer | Total | Inner           | Central | Outer | Total |
| Cáceres (11)                | 600  | —                | —       | —     | 7     | 44              | 33      | 19    | 29    |
| Donegan (12)                | 113  | 12               | 0       | 4     | 6     | 54              | 29      | 31    | 34    |
| Handley (13)                | 1000 | 12               | 7       | 4     | 8     | 50              | 46      | 22    | 35    |
| Lacour <i>et al.</i> (14)   | 703  | 11               | —       | 8     | 9     | 37              | —       | 22    | 28    |
| Livingston and Arlen (8)    | 583  | 14               | 10      | 5     | 8     | 59              | 43      | 23    | 32    |
| Sugg <i>et al.</i> (17)     | 292  | —                | —       | —     | 5     | —               | —       | —     | 44    |
| Urban and Marjani (9)       | 725  | 13               | 6       | 3     | 8     | 65              | 48      | 42    | 52    |
| Veronesi <i>et al.</i> (15) | 1085 | —                | —       | —     | 9     | —               | —       | —     | 28    |

**Status axilla & CMI+**

**Ax N0** → **CMI + 6-9%**  
**Ax N+** → **CMI + 28-52%**

**T & CMI+**

**T1-T2** → **CMI + 12-15%**  
**T3** → **CMI + 28-48%**

**pN & CMI+**

**pN0** → **CMI + 5%**  
**pN1** → **CMI + 19%**  
**pN2** → **CMI + 52%**



# CMI-STUDI RANDOMIZZATI

| Series                       | #   | Radical mastectomy<br>+ IMN irradiation* |           | #   | Radical mastectomy<br>alone |                 | Follow-up     |
|------------------------------|-----|--|-----------|-----|-----------------------------|-----------------|---------------|
|                              |     | DM                                       | OS        |     | DM                          | OS              |               |
| Fisher <i>et al.</i> (39)    | 470 | 40%                                      | 56%       | 633 | 32%                         | 62%             | 5 years       |
|                              |     |  |           |     |                             | <i>p</i> = NS   |               |
| Host <i>et al.</i> (40)      |     |  |           |     |                             |                 |               |
| Stage I                      | 170 | —  | 60%       | 186 | —                           | 70%             | 15 years      |
|                              |     |  |           |     |                             | <i>p</i> = 0.08 |               |
| Stage II                     | 95  | 34%†                                     | 42%       | 91  | 50%†                        | 44%             | 15 years      |
|                              |     |  |           |     | <i>p</i> = NS               | <i>p</i> = 0.15 |               |
| Palmer & Ribeiro (41)        |     |  |           |     |                             |                 |               |
| Node -                       | 139 | —  | 16%       | 142 | —                           | 26%             | 30 years      |
|                              |     |  |           |     |                             | <i>p</i> = 0.13 |               |
| Node +                       | 243 | —  | 8%        | 217 | —                           | 8%              | 30 years      |
|                              |     |  |           |     |                             | <i>p</i> = 0.7  |               |
| Arriagada <i>et al.</i> (42) | 41‡ | 51%                                      | 59%       | 31‡ | 35%                         | 74%             | 15 year crude |
|                              |     |  |           |     | <i>p</i> = 0.22             | <i>p</i> = 0.29 |               |
| Veronesi <i>et al.</i> (44)  | 23‡ | —  | 48% (DFS) | 23‡ | —                           | 68% (DFS)       | 10 years      |
|                              |     |  |           |     |                             | <i>p</i> = NS   |               |

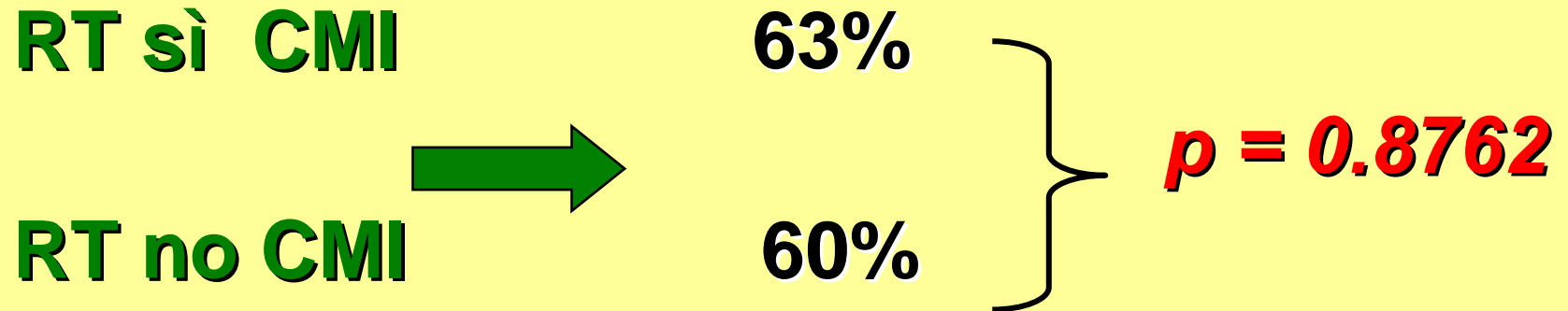
**Nessuna differenza significativa**

# STUDIO RANDOMIZZATO MULTICENTRICO

*P. Romestaing , Annual ASTRO Meeting 2009, proceedings Abs 1*

- **Fase III, RT su parete, ascella , svc  $\pm$  cmi**
- **Stadio I-II mastectomia**
- **Età > 76 aa, N+**
- **tumori centrali / interni # da N**
- **1334 pz ( 75% N +)**

## **Sopravvivenza a 10 aa**



***Nax+ vs Nax-***  
***T Qe vs Qm/I***

} ***nessuna differenza***

***CMI va irradiata se positiva***

# TRATTAMENTO : riproducibilità



# I VOLUMI

## Loco-regional conformal radiotherapy of the breast: delineation of the regional lymph node clinical target volumes in treatment position

Ivessa M. Dijkema<sup>a,\*</sup>, Pieter Hofman<sup>a</sup>, Cornelis P.J. Raaijmakers<sup>a</sup>, Jan J. Lagendijk<sup>a</sup>, Jan J. Battermann<sup>a</sup>, Berend Hillen<sup>b</sup>

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Received 22 January 2003; received in revised form 14 February 2004; accepted 26 February 2004

Lymph node region Anatomical location

**R&O 2004**

| Lymph node region | Anatomical location  |                   |   |
|-------------------|--|-------------------|---|
| Axillary LNs      |  | SC LNs            |   |
| Lateral           | Along the lateral part of the axillary v.: from the tendon of the latissimus dorsi m. to the termination of the thoracoacromial v. (medial of the pectoralis minor m.).  | Medial            | Inferior jugular nodal chain: in the carotid sheath, especially lateral and posterior of the lower internal jugular v., dorsal of sternocleidomastoid m. and caudal of the intermediate tendon of the omohyoid m. (lower border cricoid cartilage).<br>Medial part transverse cervical nodal chain: along the medial part of the transverse cervical vessels (branches of the external jugular v. and thyrocervical trunk), ventral of the scalenus anterior m., dorsal of sternocleidomastoid m. |
| Pectoral          | Around the lateral thoracic vessels: along the lateral border of the pectoralis major and minor m.   |                   | Lateral part transverse cervical nodal chain: along the lateral part of the transverse cervical vessels, lateral of the sternocleidomastoid m., ventral of the scalenus medius and levator scapulae mm., caudal and ventral of the omohyoid m.  |
| Subscapular       | Around the subscapular vessels and its thoracodorsal branches: along the lateral border of the subscapular m.  | Lateral           | Along the cephalic v. in the deltopectoral triangle (Mohrenheim's groove): between the pectoralis major m., deltoid m. and clavicle, medial of the coracoid process.  |
| Central           | Associated with the axillary vessels behind the pectoralis minor m.: centrally in the axilla.  |                   | Small LNs (1–5 mm size) lateral or medial of IMV, on the endothoracic fascia or transversus thoracis m., ventral of the parietal pleura, draining to the bronchomediastinal trunk, terminating in the jugulo–subclavian junction.   |
| Apical            | Ventral and superior of the medial part of the axillary v.: proximal of the termination of the thoracoacromial v. to the apex of the axilla, lying posterior and medial of the medial border of the pectoralis minor m. and caudal and ventral of the subclavius m., terminating in the subclavian trunk: along the subclavian v. to the jugulo–subclavian junction. | IC LNs<br><br>IMN | Along the pectoral branches of the thoracoacromial vessels, between the pectoralis major and minor m.   |
|                   |  | Interpectoral LNs |   |

# CTV DEI DRENAGGI

**Dijkema , R&O 2004**

Table 2  
Guidelines for delineating the anatomical boundaries of the regional lymph node clinical target volumes (arm in treatment position)

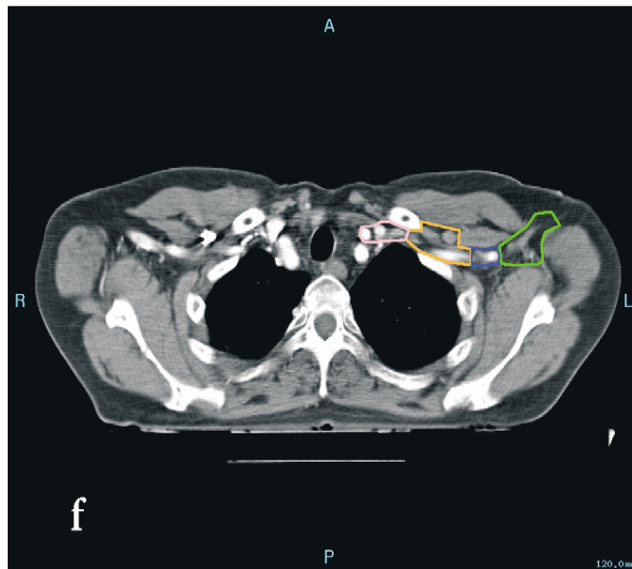
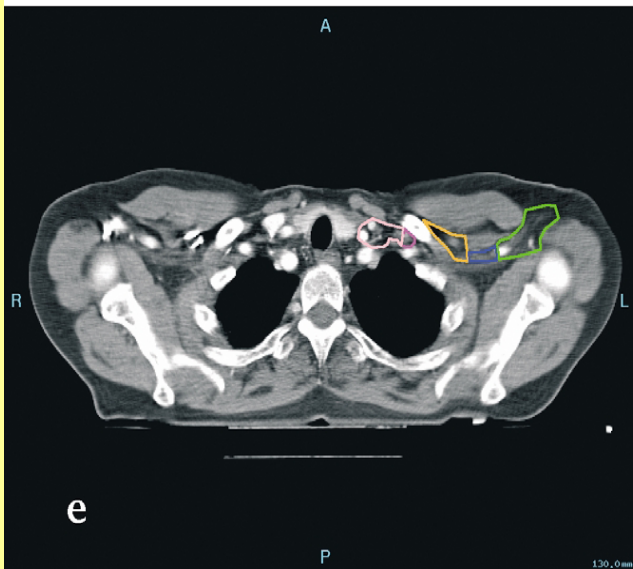
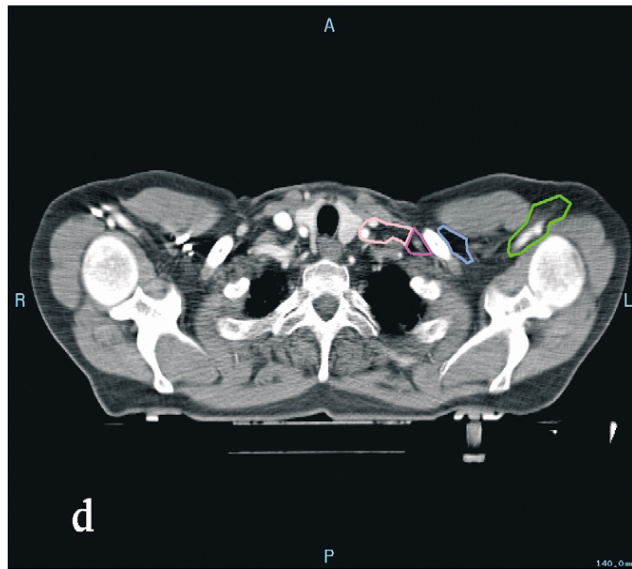
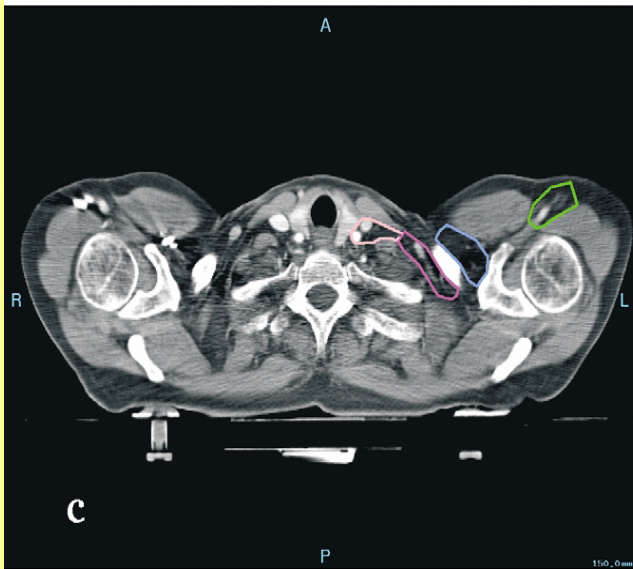
|   | Cranial                                     | Caudal   | Ventral  | Dorsal  | Lateral   | Medial  |
|---|---|--|--|---|---|---|
| Axilla level I                                | Caudal CT-slice tendon latissimus dorsi m.  | Caudal CT-slice free edge pectoralis major m, caudal CT-slice subscapular m.     | Skin <sup>a</sup>  | Dorsal border axillary vessels, subscapular m., serratus anterior m.                | Latissimus dorsi m., teres major m., subscapular m. <sup>b</sup>            | Biceps brachii m., coracobrachialis m., lateral border pectorales mm. <sup>c</sup> and breast |
| Axilla level II                               | Cranial CT-slice axillary vessels           | Caudal CT-slice free edge pectoralis minor m.                                    | Dorsal surface pectoralis minor m.                         | Dorsal border axillary vessels, rib, serratus anterior m.                           | Lateral border pectoralis minor m. <sup>c</sup>                             | Medial border pectoralis minor m. <sup>d</sup>  |
| Axilla level III (including subclavian trunk) | Caudal CT-slice coracoid process            | Caudal CT-slice axillary v.  | Dorsal surface pectoralis major m.                         | Ventral border subclavius m., dorsal border subclavian v. and axillary vessels, rib | Medial border pectoralis minor m.   | Clavicle, rib, lateral border jugulo-subclavian junction                                      |
| Medial SC LNs                                 | Caudal CT-slice cricoid cartilage           | Cranial CT-slice jugulo-subclavian junction, caudal CT-slice external jugular v. | Dorsal surface sternocleidomastoid m.                      | Dorsal border internal carotid a., ventral border scalenus anterior m.              | Lateral border sternocleidomastoid m. and scalenus anterior m.              | Medial edge internal carotid a. and internal jugular v.                                       |
| Lateral SC LNs                                | Cranial CT-slice omohyoid m.                | Caudal CT-slice external jugular v., transverse cervical vessels                 | Clavicle, skin   | Ventral surface omohyoid m., levator scapulae m., scalenus medius m.                | Clavicle, trapezius m.  | Lateral border sternocleidomastoid m. and scalenus anterior m.                                |
| IC LNs  | CT-slice caudal to deltoid m.               | Caudal CT-slice coracoid process   | Pectoralis major m., skin                                  | Clavicle, subclavius m.   | Medial border coracoid process, pectoralis minor m. and coracobrachialis m. | Skin, origin pectoralis major m. on clavicle  |
| Intepectoral LNs                              | Cranial CT-slice thoracoacromial vessels    | Caudal CT-slice pectoralis minor m.  | Dorsal surface pectoralis major m.                         | Ventral surface pectoralis minor m.   | Lateral border pectoralis minor m.  | Medial border pectoralis minor m.   |
| IMN   | Cranial CT-slice jugulo-subclavian junction | Cranial CT-slice 4th rib   | Dorsal surface pectoralis major m., dorsal surface sternum | Pleura or 5 mm fat tissue dorsal of IMV   | 5 mm lateral of IMV, lateral border of brachiocephalic v.                   | 5 mm medial of IMV, medial border brachiocephalic v.  |

LNs, lymph nodes; SC, supraclavicular; IC, infraclavicular; m., muscle; mm., muscles; a., artery; v., vein; IMN, internal mammary nodes; IMV, internal mammary vessels.

<sup>a</sup> ≤ 5 mm ventral of axillary vessels.

<sup>b</sup> ≤ 5 mm latero-dorsal of thoracodorsal and axillary vessels.

<sup>c</sup> Position of lateral thoracic vessels.



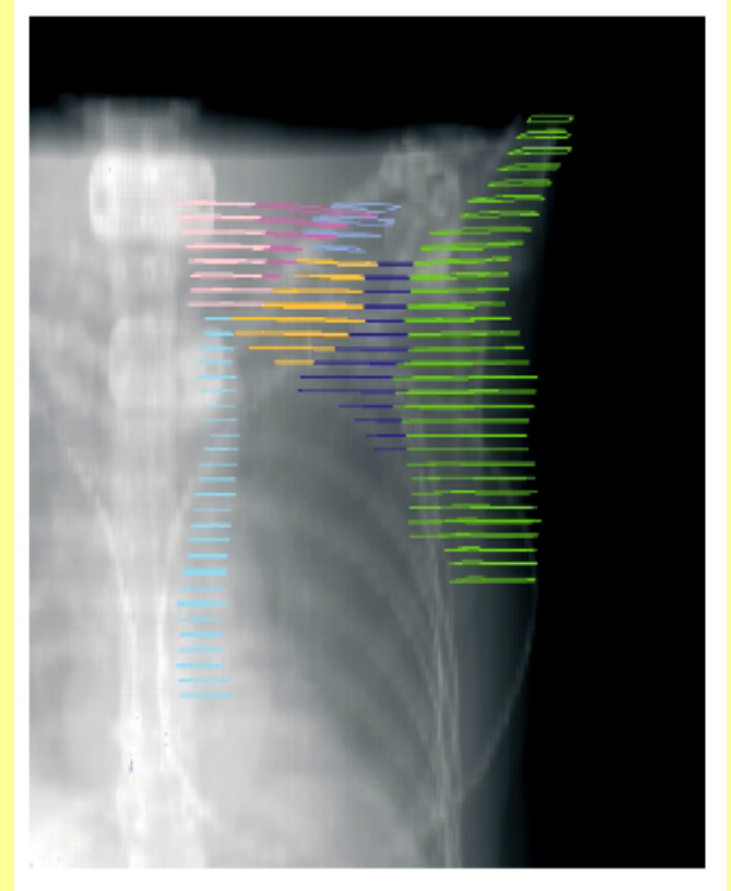
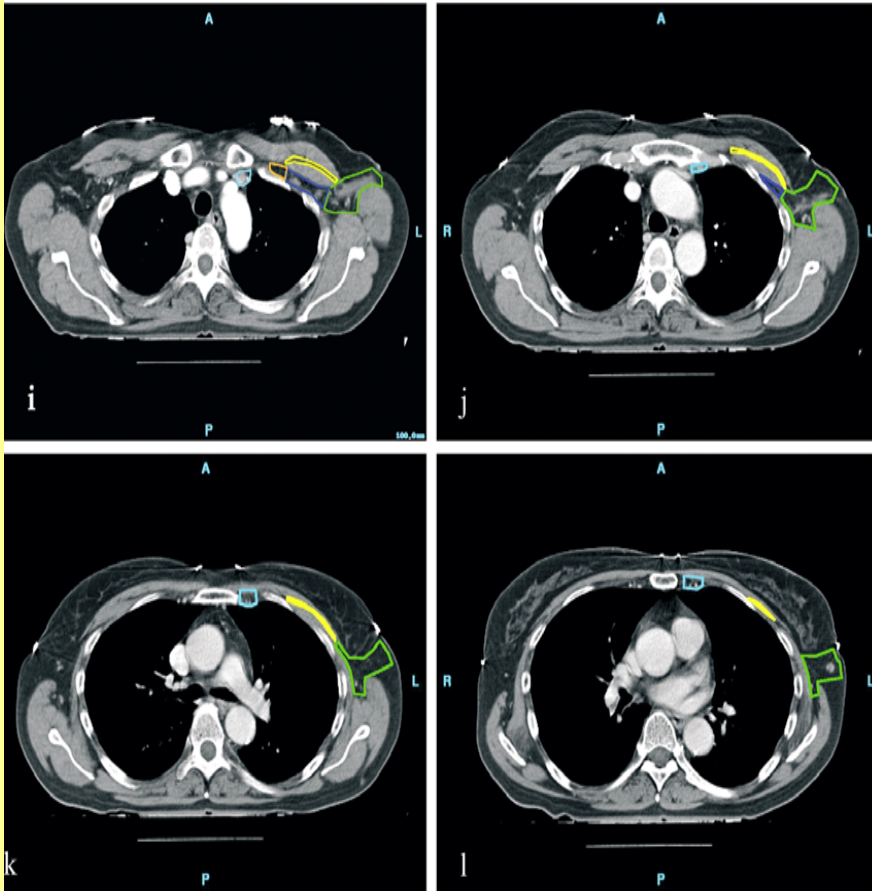
svcmed

svclat

infraclv

infpett

cmi



***Dijkema , R&O 2004***



# Breast Cancer Atlas for Radiation Therapy Planning: Consensus Definitions



## Overlying principles: Nodal volumes

### Regional nodal CTV:

- Nodal volumes contoured for targeting will depend on the specific clinical case
- Considers consensus definitions of anatomical borders (see table)
- The three levels of the axilla can overlap caudal to cranial
- “Axillary apex” was considered level III of the axilla

## Contouring Comments: Regional Nodal Volumes

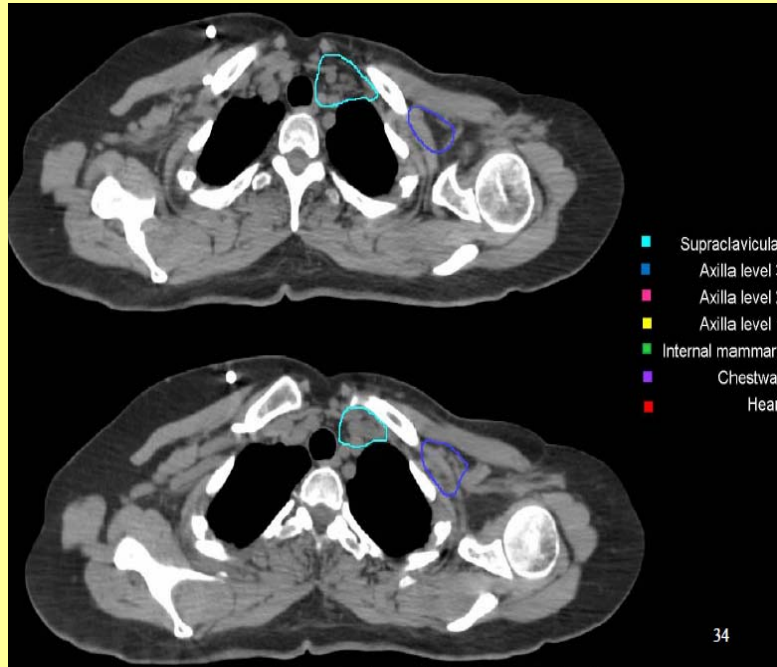
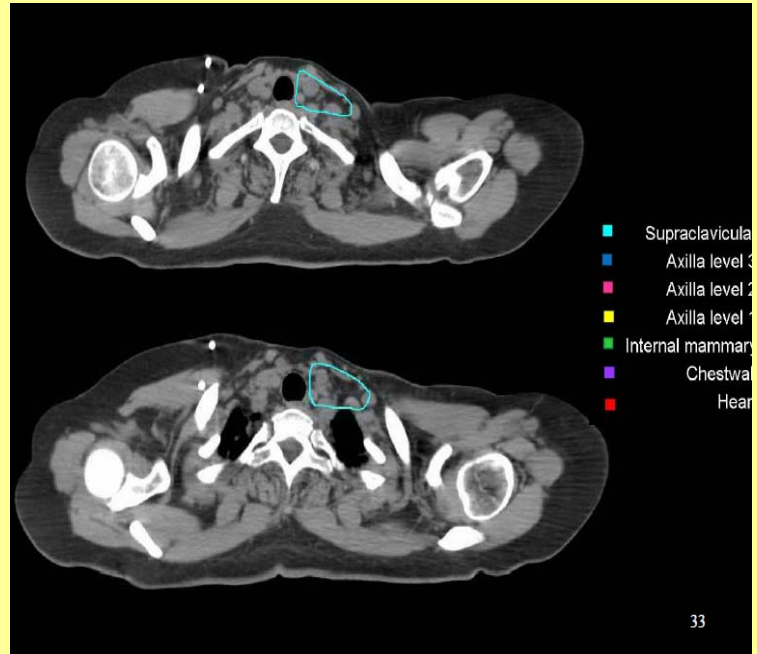
- a.** Supraclavicular caudal border meant to approximate the superior aspect of the breast/ chestwall field border
- b.** Axillary level I caudal border is clinically at the base of the anterior axillary line
- c.** Axillary level II caudal border is the same as the cranial border of level 1
- d.** Axillary level III caudal border is the same as the cranial border of level II
- e.** Internal Mammary lymph nodes: encompass the internal mammary/ thoracic vessels

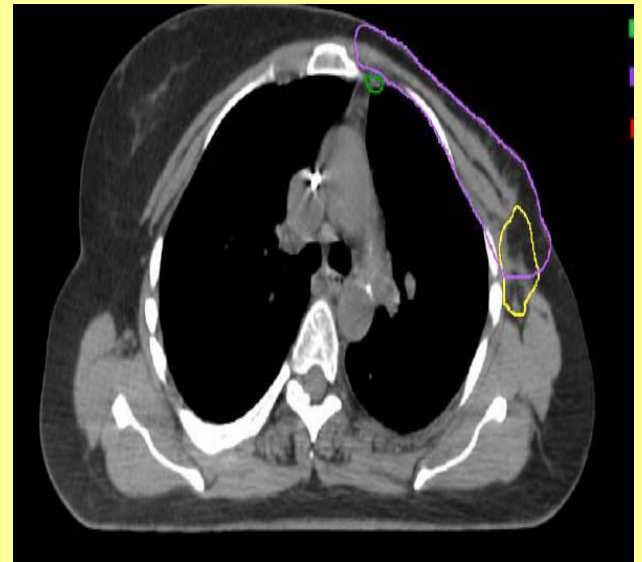
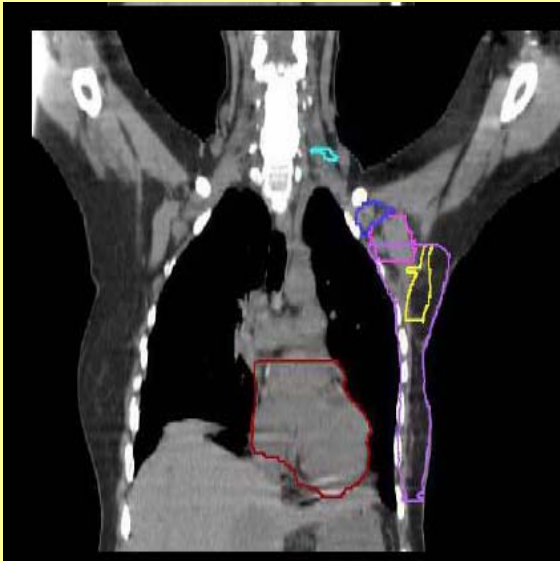
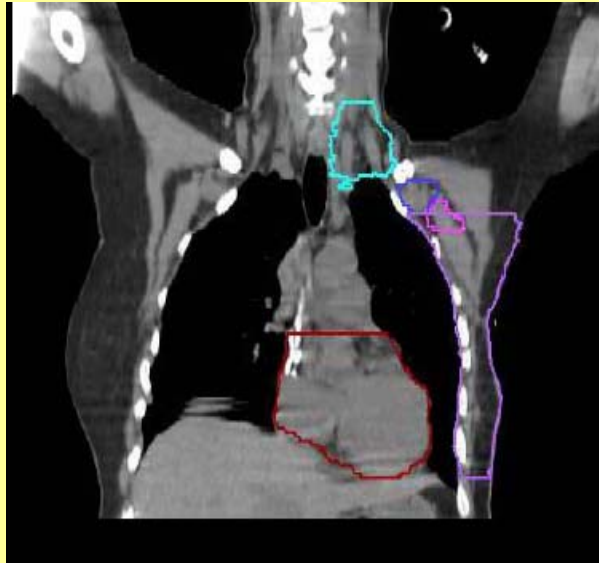
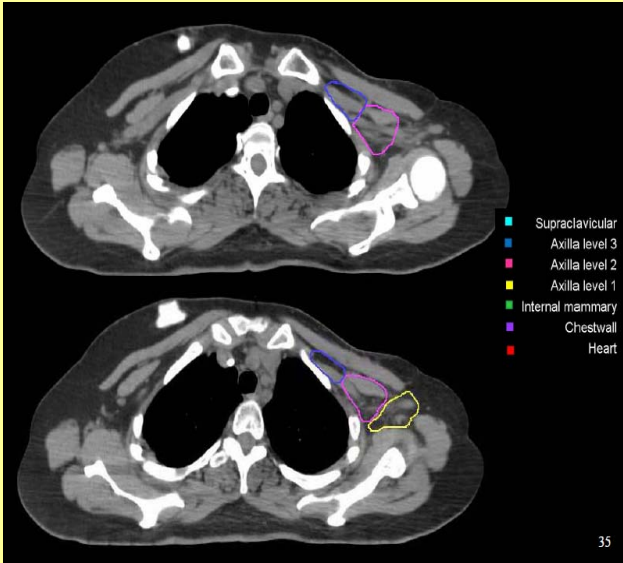
### Regional Nodal Contours: Anatomical Boundaries

|                  | <i>Cranial</i>                                       | <i>Caudal</i>  | <i>Anterior</i>  | <i>Posterior</i>                     | <i>Lateral</i>   | <i>Medial</i>                   |
|------------------|--|--|--|--------------------------------------|--|---------------------------------|
| Supra-clavicular | Caudal to the cricoid cartilage                      | Junction of brachioceph.-axillary vns./ caudal edge clavicle head <sup>a</sup> | Sternocleido mastoid (SCM) muscle (m.)                               | Anterior aspect of the scalene m.    | <b>Cranial:</b> lateral edge of SCM m.<br><b>Caudal:</b> junction 1 <sup>st</sup> rib-clavicle | Excludes thyroid and trachea    |
| Axilla-Level I   | Axillary vessels cross lateral edge of Pec. Minor m. | Pectoralis (Pec.) major muscle insert into ribs <sup>b</sup>                   | Plane defined by: anterior surface of Pec. Maj. m. and Lat. Dorsi m. | Anterior surface of subscapularis m. | Medial border of lat. dorsi m.   | Lateral border of Pec. minor m. |
| Axilla-level II  | Axillary vessels cross medial edge of Pec. Minor m.  | Axillary vessels cross lateral edge of Pec. Minor m. <sup>c</sup>              | Anterior surface Pec. Minor m.                                       | Ribs and intercostal muscles         | Lateral border of Pec. Minor m.  | Medial border of Pec. Minor m.  |
| Axilla-level III | Pec. Minor m. insert on cricoid                      | Axillary vessels cross medial edge of Pec. Minor m. <sup>d</sup>               | Posterior surface Pec. Major m.                                      | Ribs and intercostal muscles         | Medial border of Pec. Minor m.   | Thoracic inlet                  |
| Internal mammary | Superior aspect of the medial 1 <sup>st</sup> rib.   | Cranial aspect of the 4 <sup>th</sup> rib                                      | - e.   | - e.                                 | - e.   | - e.                            |

# RTOG

## RADIATION THERAPY ONCOLOGY GROUP





# PLANNIG 3D

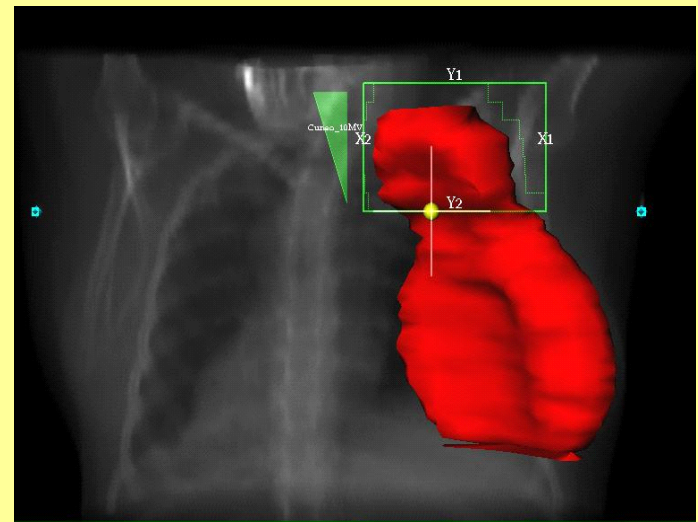
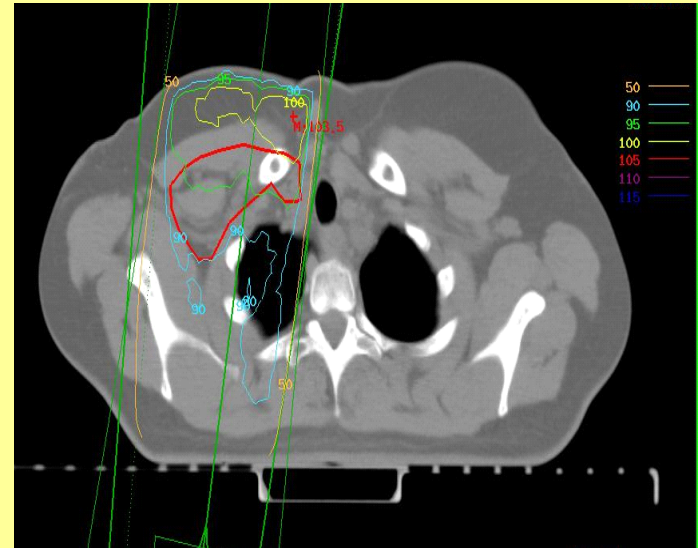
MM + SOV

TECNICA EMICAMPI  
ISOCENTRICA

2 CAMPI CONTRAPPOSTI  
ANGOLATI

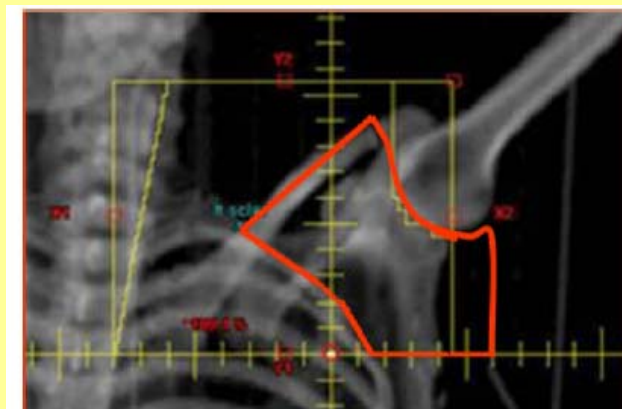
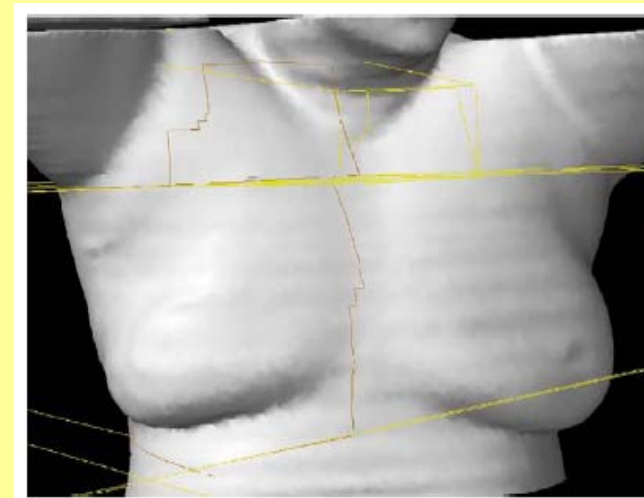
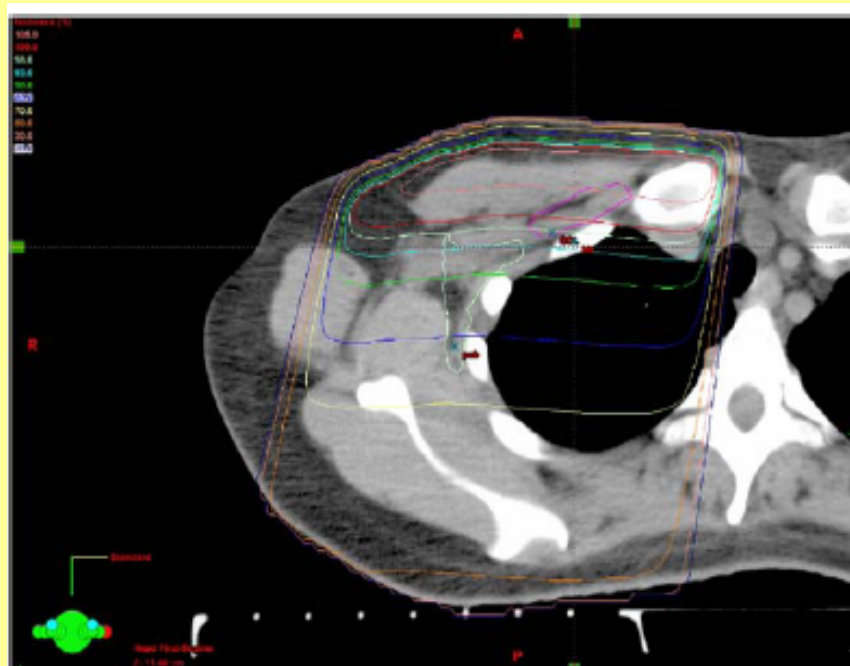
FOTONI 6-10 MV

*2 Gy / 24 fr*

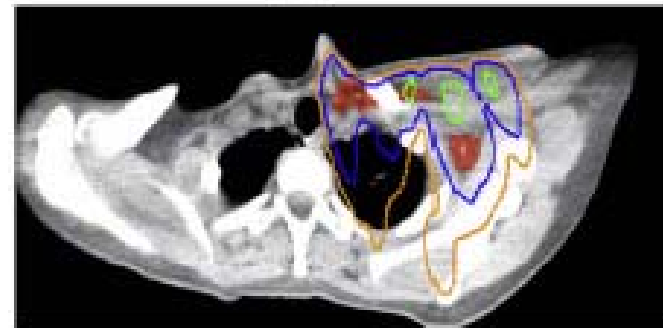
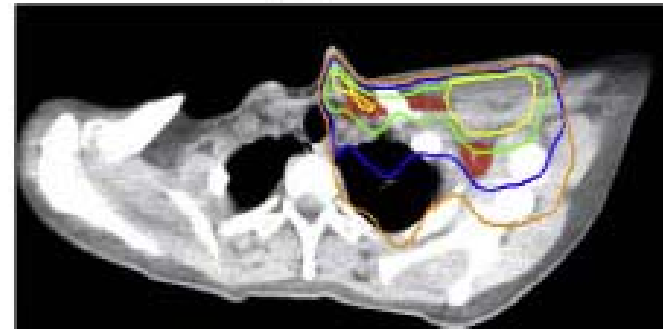
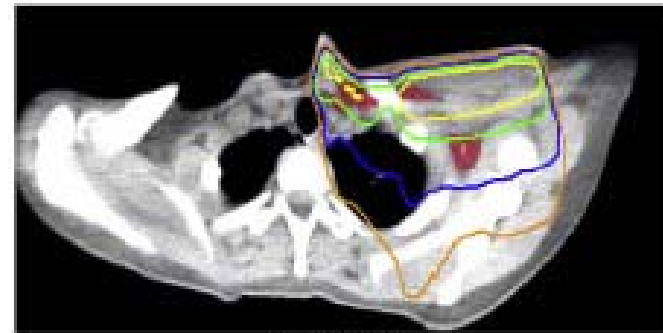
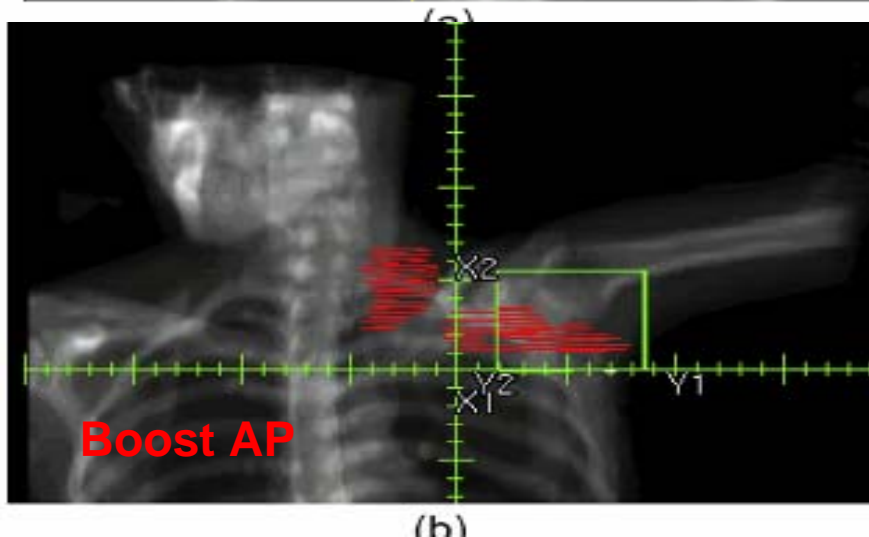
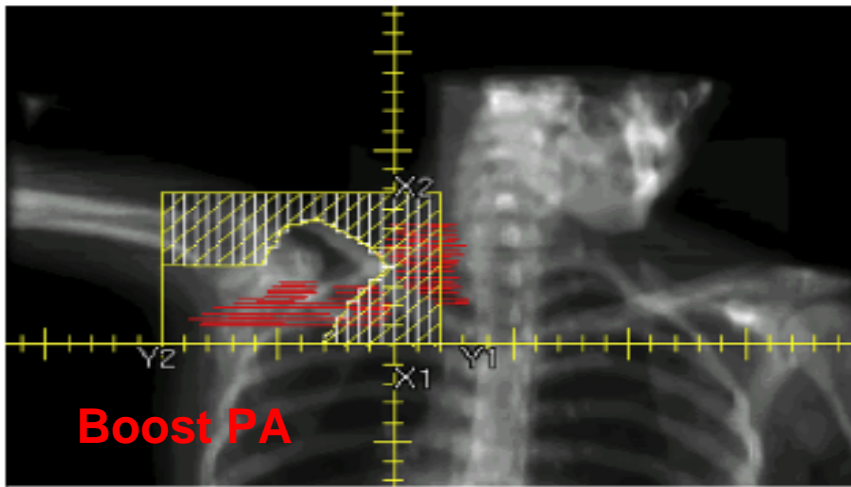


# SOVRACLAVEARE+ASCELLA

Moran, SRO 2009

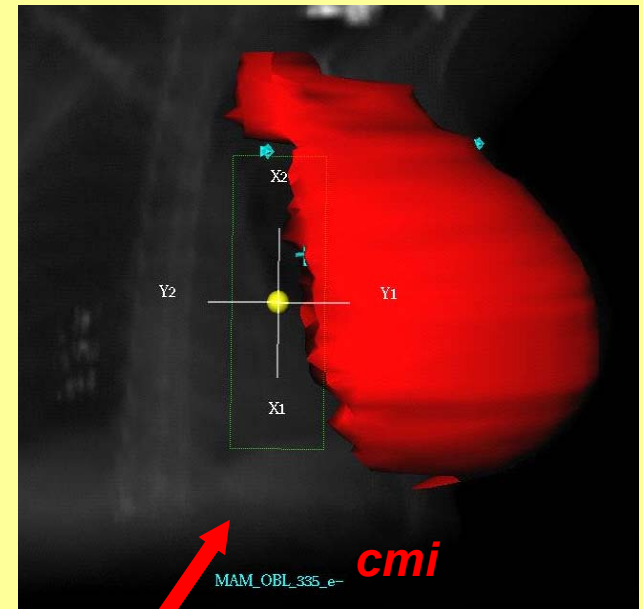
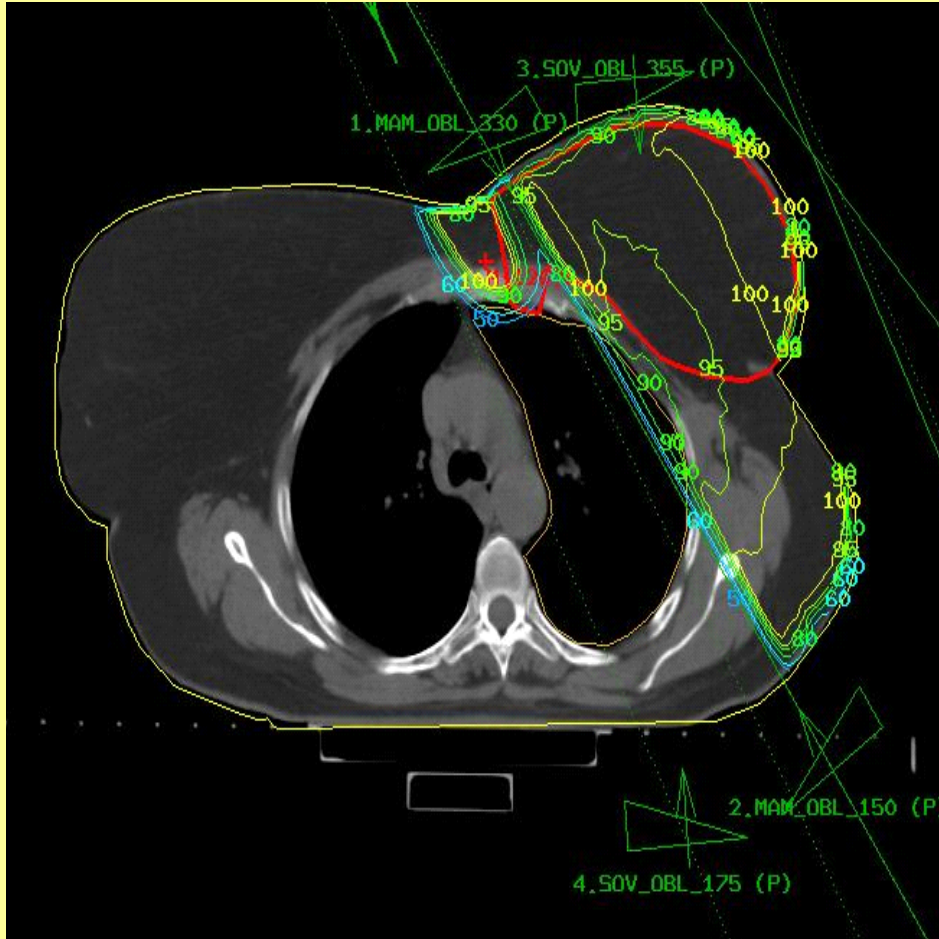


BREAST CANCER REGIONAL RADIATION FIELDS FOR SUPRACLAVICULAR AND AXILLARY LYMPH NODE TREATMENT: IS A POSTERIOR AXILLARY BOOST FIELD TECHNIQUE OPTIMAL?



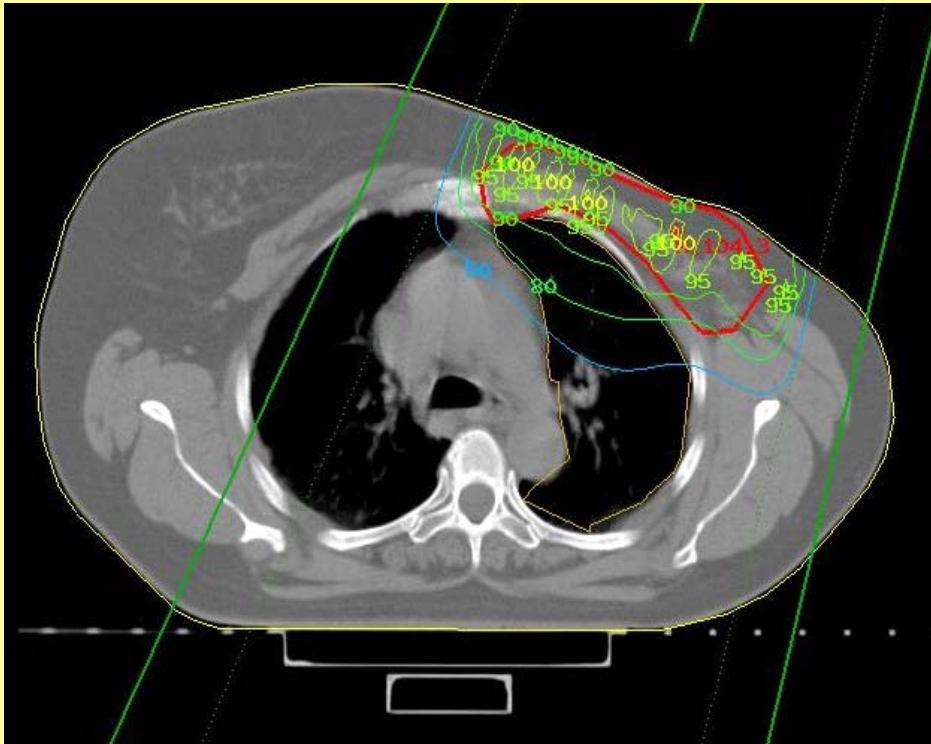
# CATENA MAMMARIA INTERNA

**FOTONI + ELETTRONI / ELETTRONI**



# CATENA MAMMARIA INTERNA

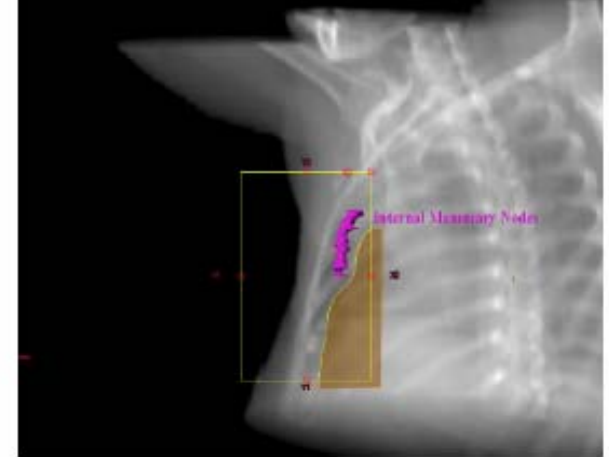
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SOLO CON ELETTRONI**



**PARETE e CATENA MAMMARIA INTERNA  
CON TECNICA MISTA: FOTONI + ELETTRONI**



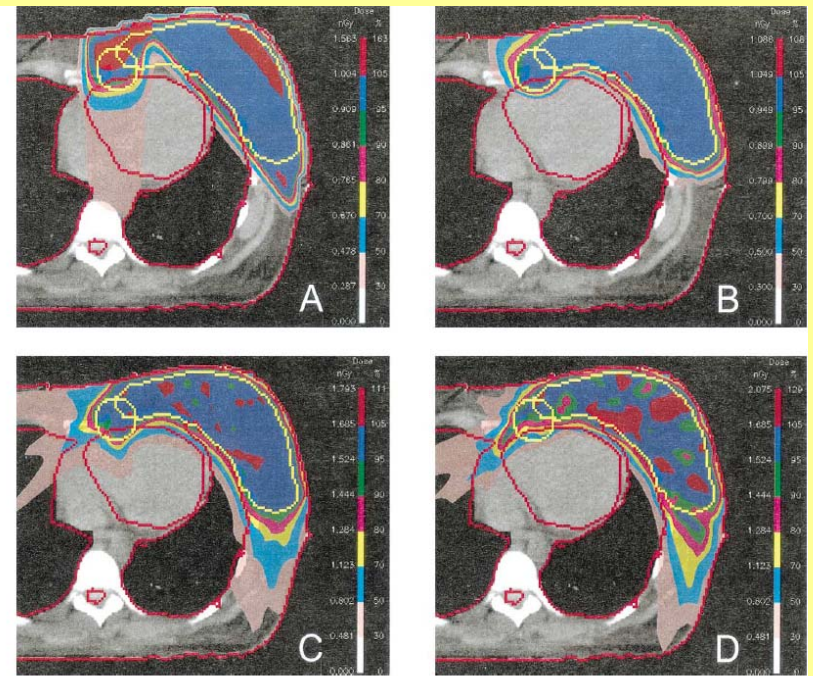
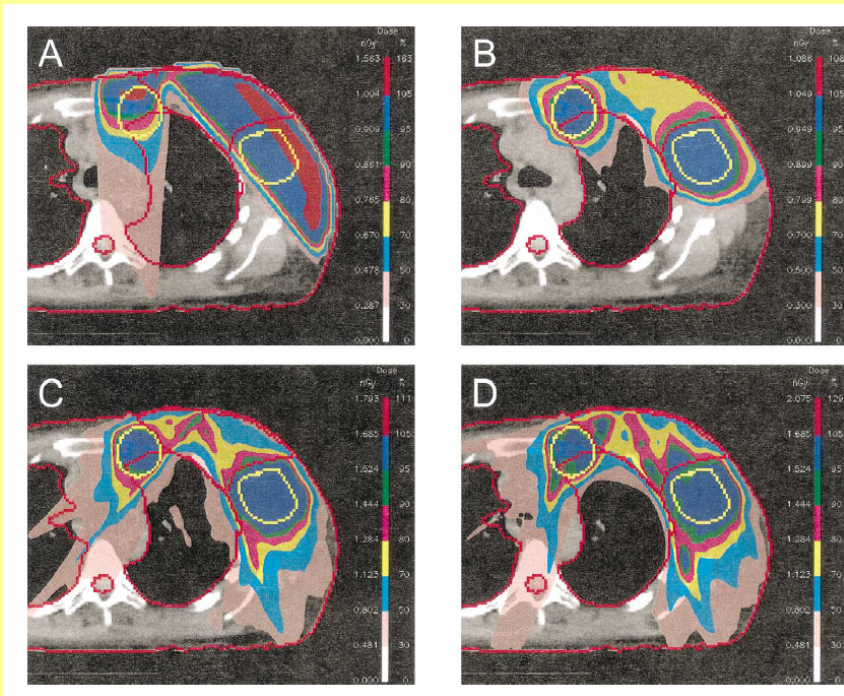
**CAMPI TANGENZIALI X**

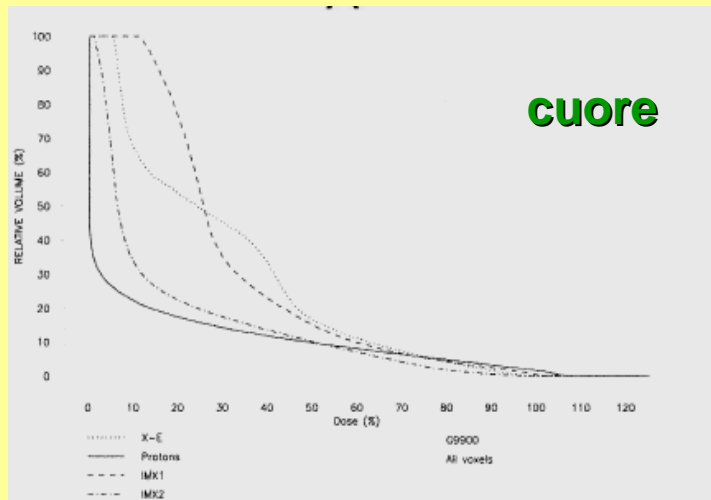
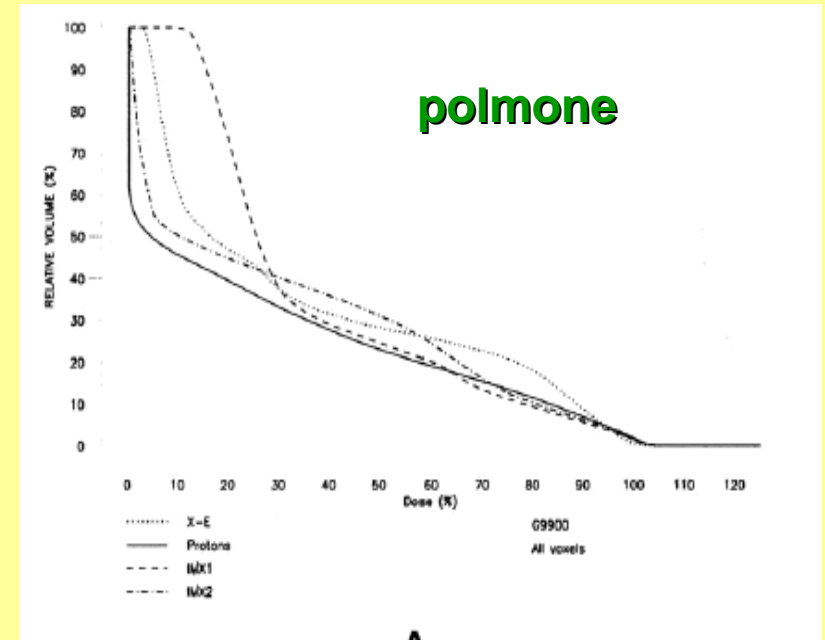
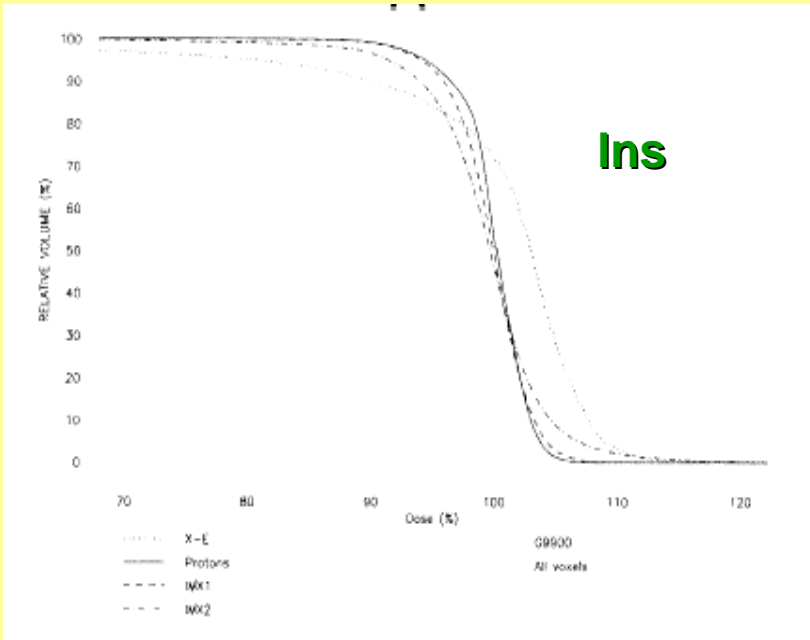




# IMRT & PROTONI

A = CONVENZIONALE  
B = PROTONI  
C = IMRT 1  
D = IMRT 2





## IMRT

**Buona copertura ma perdita di dose nel preservare gli OARs**

## PROTONI

**Migliore copertura e risparmio OARs**

# TOSSICITA'

**OAR**

**DANNO**

**PLESSO BRACHIALE**

**TESTA OMERALE**

**VENTRICOLO SX**

**RT AX - SOV**

**RT CMI**

**EDEMA ARTO**

**EDEMA BASE COLLO**

**ISCHEMIA CARDIACA**

British Journal of Cancer (2009) 100, 811–816  
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www.bjcancer.com

Acta Oncologica, 2010; 49: 24–34

**informa**  
healthcare

ORIGINAL ARTICLE

Radiation to supraclavicular and internal mammary lymph nodes in breast cancer increases the risk of stroke

Toxicity at three years with and without irradiation of the internal mammary and medial supraclavicular lymph node chain in stage I to III breast cancer (EORTC trial 22922/10925)

G Nilsson<sup>8,1</sup>, L Holmberg<sup>2,3</sup>, H Garmo<sup>2,3</sup>, A Terent<sup>4</sup> and C Blomqvist<sup>1</sup>

OSCAR MATZINGER<sup>1,2</sup>, IRMA HEIMSOTH<sup>3</sup>, PHILIP POORTMANS<sup>4</sup>,

**Table 4** ORs and 95% CIs for stroke and subtypes of stroke associated with adjuvant therapy

|                              | Cases |        | Controls |        | Stroke, age adjusted |              | Cerebral haemorrhage, age adjusted |              | Ischaemic stroke and ill-defined cerebrovascular lesion, age adjusted |              |
|------------------------------|-------|--------|----------|--------|----------------------|--------------|------------------------------------|--------------|---|--------------|
|                              | N     | (%)    | N        | (%)    | OR                   | 95% CI       | OR                                 | 95% CI       | OR  | 95% CI       |
| RT                           |       |        |          |        |                      |              |                                    |              |   |              |
| No                           | 125   | (44.3) | 91       | (32.3) | ref                  |              | ref                                |              | ref   |              |
| Yes                          | 157   | (55.7) | 191      | (67.7) | 0.85                 | (0.56, 1.30) | 1.39                               | (0.38, 5.07) | 0.79  | (0.50, 1.24) |
| RT                           |       |        |          |        |                      |              |                                    |              |   |              |
| No RT                        | 127   | (45.0) | 92       | (32.6) | ref                  |              | ref                                |              | ref   |              |
| RT, except IMC/SCL           | 58    | (20.6) | 97       | (34.4) | 0.45                 | (0.25, 0.79) | 1.52                               | (0.35, 6.59) | 0.34  | (0.18, 0.65) |
| RT to IMC/SCL                | 97    | (34.4) | 93       | (33.0) | 1.32                 | (0.80, 2.19) | 1.23                               | (0.25, 5.96) | 1.33  | (0.77, 2.28) |
| RT                           |       |        |          |        |                      |              |                                    |              |   |              |
| No RT and RT, except IMC/SCL | 185   | (65.6) | 189      | (67.0) | ref                  |              | ref                                |              | ref   |              |
| RT to IMC/SCL                | 97    | (34.4) | 93       | (33.0) | 1.78                 | (1.13, 2.82) | 1.00                               | (0.25, 4.01) | 1.93  | (1.18, 3.17) |

**Table 6** ORs and 95% CIs for stroke in association with daily fraction radiation doses

|  | Case | Control | OR   | Age adjusted |
|--|------|---------|------|--------------|
| <i>Daily fraction radiation dose IMC</i> |      |         |      |              |
| No RT                                    | 184  | 189     | ref  |              |
| ≤2.5 Gy                                  | 20   | 34      | 0.56 | (0.24, 1.31) |
| 2.6–3.9 Gy                               | 64   | 49      | 2.61 | (1.48, 4.60) |
| ≥4 Gy                                    | 11   | 10      | 3.05 | (0.97, 9.58) |
| Unclear                                  | 3    | 0       | —    | —            |
| <i>Daily fraction radiation dose SCL</i> |      |         |      |              |
| No RT                                    | 183  | 190     | ref  |              |
| ≤2.5 Gy                                  | 19   | 33      | 0.54 | (0.23, 1.29) |
| 2.6–3.9 Gy                               | 45   | 36      | 2.14 | (1.15, 3.99) |
| ≥4 Gy                                    | 32   | 23      | 4.06 | (1.85, 8.94) |
| Unclear                                  | 3    | 0       | —    | —            |

CI = confidence interval; IMC = internal mammary chain; OR = odds ratio; RT = radiotherapy; SCL = supraclavicular.

**Rischio stroke correlata al frazionamento giornaliero non alla lateralita di malattia**

**British Journal of Cancer 2009**

Table VI. Correlation between toxicity and WHO performance status deterioration at three years

| Deterioration by year 3                        | No Change/<br>improvement<br>(N=3056) | Deterioration<br>(N=285) | OR   | 95% CI    | P-value    |
|--|---------------------------------------|--------------------------|------|-----------|------------|
|  | N (%)                                 | N (%)                    |      |           |            |
| <b>Any lung toxicity</b>                       |                                       |                          |      |           |            |
| No   | 2972 (91.5)                           | 276 (8.5)                |      |           |            |
| Yes  | 84 (90.3)                             | 9 (9.7)                  | 1.19 | 0.59-2.41 | 0.62       |
| <b>Lung Fibrosis (to year 3)</b>               |                                       |                          |      |           |            |
| No   | 2996 (91.5)                           | 280 (8.5)                |      |           |            |
| Yes  | 56 (91.8)                             | 5 (8.2)                  | 1.02 | 0.40-2.59 | 0.96       |
| Missing  | 4 (100.0)                             | 0 (0.0)                  |      |           |            |
| <b>Cardiac Fibrosis (to year 3)</b>            |                                       |                          |      |           |            |
| No   | 3038 (91.4)                           | 285 (8.6)                |      |           | Too small  |
| Yes  | 11 (100.0)                            | 0 (0.0)                  |      |           | sample for |
| Missing  | 7 (100.0)                             | 0 (0.0)                  |      |           | testing    |
| <b>Evidence of cardiac disease (to year 3)</b> |                                       |                          |      |           |            |
| No   | 2989 (91.9)                           | 265 (8.1)                |      |           |            |
| Yes  | 38 (76.0)                             | 12 (24.0)                | 3.71 | 1.90-7.24 | <0.0001    |
| Missing  | 29 (78.4)                             | 8 (21.6)                 |      |           |            |

**Tossicità polmonare**

**4% vs 1.3 %**

**$p < 0.0001$**

**Tossicità cardiaca**

**0.3% vs 0.4%**

**$P = 0.55$**

**Nessun impatto sul PS**

**EORTC 22922 Acta Oncologica 2010**

# CONCLUSIONI

## EDITORIALS

### More Evidence That Locoregional Radiation Therapy Improves Survival: What Should We Do?

*Timothy Whelan, Mark Levine*

Journal of the National Cancer Institute, Vol. 97, No. 2, January 19, 2005



**grazie**