

# Conservative Treatment Versus Mastectomy in Breast Cancer Tumors With Macroscopic Diameter of 20 Millimeters or Less

## The Experience of the Institut Gustave-Roussy

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A clinical trial was conducted at the Institut Gustave Roussy between October 1972 and December 1980 to compare mastectomy with local excision plus Cobalt irradiation, in patients with breast cancer tumors of 20 mm in diameter or less at macroscopic examination. Low-axillary dissection and extemporaneous histologic examination were carried out for all patients. If one or more positive nodes were found, complete axillary dissection was performed. The study included 179 patients. No significant difference was detected in either overall or relapse-free survival between the two groups, although the conservatively treated group showed slightly better results. The results of conservative treatment were esthetically satisfactory in 92% of the cases. The trial included a second randomization for the patients with positive axillary nodes to assess the value of nodal area irradiation; 72 patients were studied in this part of the trial. No significant differences were found between the two groups after adjustment for the number of positive axillary nodes, although the no-nodal irradiation group showed better results and less complications than the nodal irradiation group.

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**D**URING THE LAST 2 decades, the aim of research in early breast cancer treatment has been not only to increase long-term survival but also to improve the quality of survival by obtaining better esthetic results and lower morbidity. Such goals could be achieved by the reduction of surgery and/or radiotherapy. As regards surgery, some authors have reported their experiences with a conservative treatment for patients with small tumors,<sup>1-7</sup> but these studies were not controlled. Atkins and coworkers and Hayward<sup>8,9</sup> were the first to carry out a comparative trial of conservative therapy and mastectomy. They found no difference in survival after 10 years of follow-up, but observed increased local recurrence in the conservatively treated group. This was probably due to the fact that the trial was initiated 20 years ago, and therefore patients could not have benefitted from the most recent advances in radiotherapy. In addition, the authors had included patients with breast cancer tumors of 50 mm or less (T1, T2, N0, N1a, N1b, M0 in TNM system), and tumors

between 20 and 50 mm may be too large to be treated conservatively. Another recent study on patients with tumors of less than 20 mm<sup>10</sup> did not show any survival difference between conservative treatment and mastectomy. The conservative treatment in this study was a quadrantectomy with systematic complex axillary dissection.

As regards reducing nodal radiotherapy, several studies have been carried out, but none of them concerned only patients with tumors of 20 mm or less treated by conservative surgery. Moreover, the results of these studies are contradictory; certain reports show that radiotherapy decreases recurrence without modifying survival,<sup>11-13</sup> while others show that radiotherapy can also decrease the incidence of metastases and mortality.<sup>14-15</sup>

We report the results of a randomized trial, proposed by the World Health Organisation in 1971, comparing tumorectomy plus breast irradiation *versus* mastectomy, and for the patients with positive axillary nodes, systematic nodal irradiation *versus* no nodal irradiation.

### Material and Methods

Patients with unilateral breast cancer tumors of 20 mm or less at mammography, T1 or small T2, N0, N1a or N1b, M0, in TNM system, were considered for inclusion

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TABLE 1. Planning of the Trial: Patients with Breast Cancer Tumors of 20 MM or Less at Macroscopic Examination

	September 1972 to October 1979 First randomization		November 1979 to December 1980 No randomization			Total
<b>Level one</b>						
Surgical treatment	Tumorectomy Mastectomy		Systematic tumorectomy			
No. of patients in level one	89	91	NA			179
No. of patients N+	29	29	14			72
<b>Level two</b>			Second randomization if N+			
Nodal radiotherapy	No	Yes	No	Yes	No	Yes
No. of patients in level	11		14	15	6	8
		18				41

NA: not applicable.

in the trial. Patients over 70 years of age, pregnant women, those unable to receive extended surgery, and those who could not be followed were excluded from the study.

All eligible patients underwent an extemporaneous examination of their tumors. Only the patients with a tumor of 20 mm or less at macroscopic examination were randomized to be treated either by mastectomy or by local excision plus breast irradiation (details given later). The mastectomy did not include the excision of the pectoral muscles. Tumorectomy consisted of the removal of the tumor with a margin of 2 cm of glandular tissue. In both groups, low-axillary dissection and extemporaneous histologic examination of a minimum of seven nodes were performed; if one or more positive nodes were detected, complete axillary dissection was undertaken.<sup>16</sup> There were two levels of randomization (Table 1).

#### Level One

At first level compared mastectomy with tumorectomy. One hundred seventy-nine patients were included between September 1972 and October 1979; 88 were treated with mastectomy, and 91 with tumorectomy.

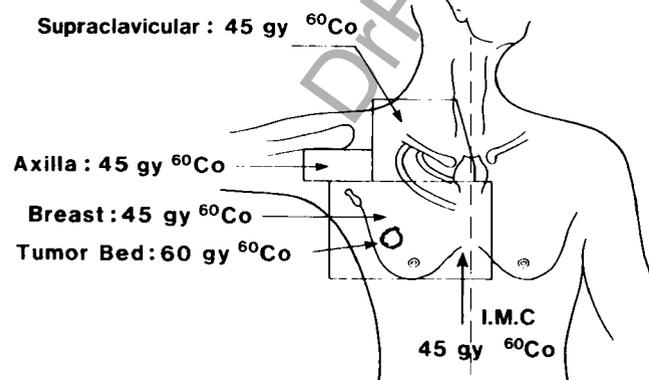


FIG. 1. Technique of irradiation: target volumes and doses.

#### Level Two

For patients with positive axillary nodes, the second level compared systematic postoperative nodal irradiation with no nodal irradiation.

Seventy-two patients were included in this part of the trial in two stages. Between September 1972 and October 1979, the 58 patients with positive axillary nodes who had been included in the first level of the study were included in the second level. In October 1979, published reports and our preliminary results led us to abandon the practice of mastectomy for the patients with breast cancer tumors of 20 mm or less, and after October 1979 all these patients underwent tumorectomy. Between November 1979 and December 1980, 14 patients with positive axillary nodes treated by systematic tumorectomy were included in the second level. Overall, 41 patients were given irradiation to the nodal areas, and 31 were not (Table 1).

Radiotherapy was delivered to the breast and nodal areas (axillary, subclavicular, and internal mammary nodes) using a Cobalt 60 teletherapy unit (Fig. 1). The local and regional dose administered was 45 Gy (4500 rad) in 18 sessions over 1 month. A booster dose of 15 Gy (1500 rad) was given to the tumor bed in six sessions, usually with the same apparatus, but some medial tumors were treated with an electron beam. The total dose was therefore 60 Gy (6000 rad) in 24 sessions over 6 weeks. The fields are shown in Figure 2.

For all patients with positive axillary nodes, the nodes and breast (only for patients having undergone a tumorectomy) were irradiated 3 times a week, by an anterior supraclavicular and axillary field of 2.5 Gy (250 rad); once a week, by an anterior supraclavicular field of 2.5 Gy (250 rad), and a posterior axillary field of the same dose. These two fields overlapped by a variable volume for some patients; 4 times a week, by two tangential fields of 2.5 Gy (250 rad) for the irradiation of the breast and the internal mammary chain.

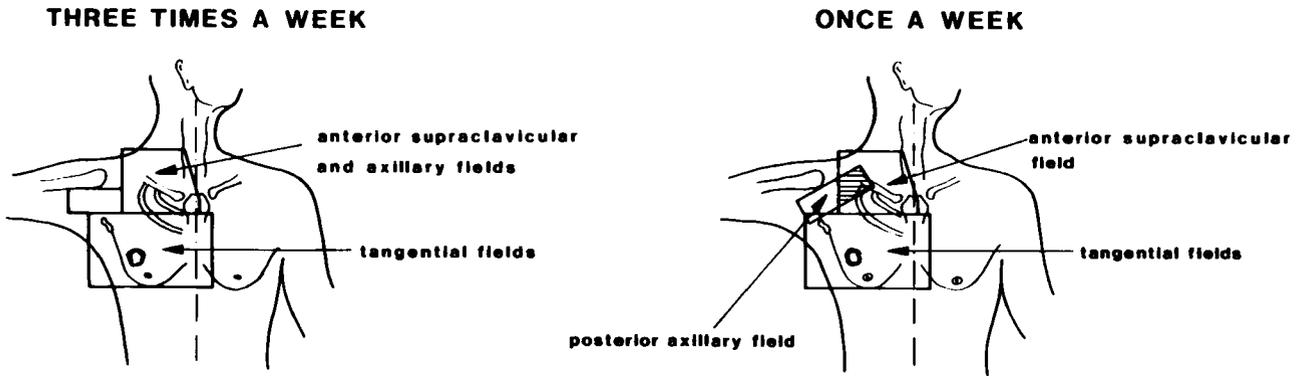


FIG. 2. Technique of irradiation: fields.

For those patients with negative axillary nodes, who had received tumorectomy, only the two tangential fields were employed. Patients who had negative nodes and who had undergone mastectomy received no radiotherapy.

**Results**

*First Randomization: Comparison of Conservative Treatment with Mastectomy*

The characteristics of the 179 patients included in level 1 are described in Table 2. These characteristics did not differ between the two groups of patients. Contrary to the protocol, 9 patients (4 in the conservatively treated group and 5 in the mastectomy group) had tumors between 21 and 25 mm, and 36 patients (17% in the tumorectomy group and 24% in the mastectomy group) with negative axillary nodes did not undergo low-axillary dissection, but received systematic axillary dissection.

Ninety-five percent of the patients have been followed

for at least 3 years, and 66% for at least 5 years. Survival curves and disease-free survival curves (life-table method) are given in Figures 3 and 4. All the logrank tests are adjusted for number of positive axillary nodes (none, 1-3, 4+). There is no significant difference between the two types of treatment. Nevertheless, the conservatively treated group did fare slightly better than the mastectomy group; 5-year survival rates are 95% versus 91%, and 5-year disease-free survival rates are 85% versus 74%, respectively. Table 3 shows the cases of treatment failure (local recurrences and metastases); there is no significant difference between the two treatments, but local recurrences and distant metastases are lower in the conservatively treated group than in the mastectomy group.

Among the patients treated with tumorectomy the esthetic result on the breast was judged excellent in 32% of the patients, good in 60% (slight retraction or alteration in position of the breast), and poor in 8% of the cases (4% with postirradiation sclerosis, and 4% with relatively extensive surgery).

TABLE 2. Characteristics of the Patients: First Randomization

	Tumorectomy (n = 88)	Mastectomy (n = 91)
Age mean +/- SD	51.4 +/- 9.8 yr	51.8 +/- 9.1 yr
Clinical dimension of tumor mean +/- SD	17.0 +/- 5.5 mm	17.4 +/- 6.3 mm
Percent of cases with internal or medial tumor localization	42%	43%
Histologic dimension of tumor mean +/- SD	15.7 +/- 3.8 mm	15.6 +/- 4.1 mm
Percent of cases by no. of positive axillary nodes:		
none	66%	65%
one to three	26%	24%
four or more	8%	11%
Percent of cases with Bloom 3	22%	27%

n = number.

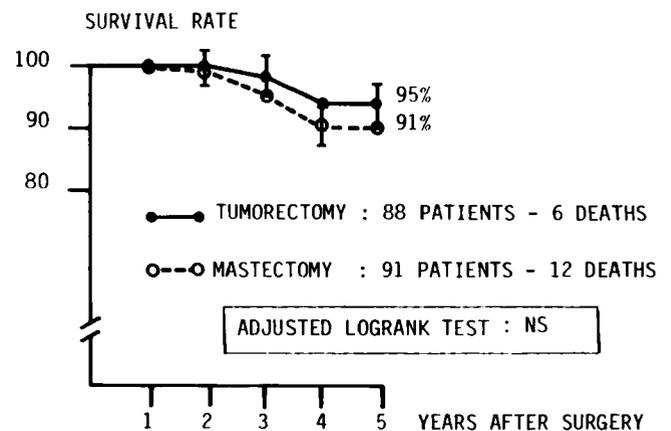


FIG. 3. Survival curves by surgical treatment.

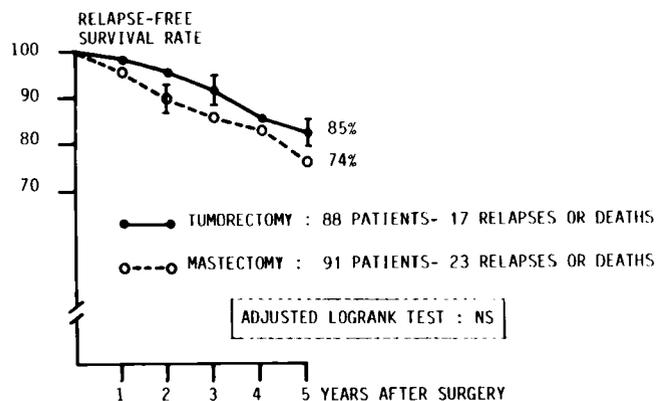


FIG. 4. Relapse-free survival by surgical treatment.

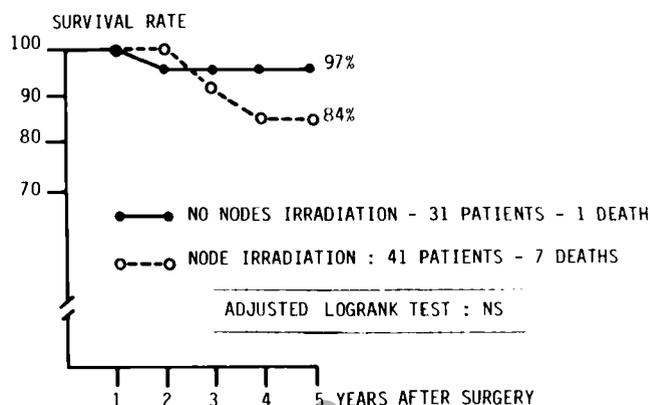


FIG. 5. Survival curves by lymph node irradiation.

**Second Randomization: Nodal Irradiation Versus No Nodal Irradiation**

The characteristics of the 72 patients included in level 2 are given in Table 4. In the nodal irradiation group, the patients were significantly younger than the patients in the other group (49.5 versus 54.4 years;  $P = 0.05$ ).

More irradiated patients had four or more positive axillary nodes (29% versus 16%) and Bloom grade 3 (32% versus 23%) than nonirradiated patients. However, these two differences are not significant.

Seventy-seven percent of the patients have been followed for 3 years, and 49% for 5 years. Survival curves and disease-free survival curves (life-table method) are given in Figures 5 and 6. There is no significant difference between the two treatments (longrank-test adjusted for

number of positive axillary nodes (three or less versus four or more), but not adjusted for age or Bloom grading because these factors were not found to be prognostic in the study). More distant metastases and less local recurrences occurred in the nodal irradiation group (Table 5), but these differences are not significant after adjustment for number of positive nodes.

**Complications**

Three of the 118 patients with negative axillary nodes (59 treated by tumorectomy, and 59 by mastectomy) had complications. One patient in the conservatively treated group experienced minor respiratory disorders; two patients in the mastectomy group developed lymphedema of the arm with functional impairment, but both had undergone complete axillary dissection (contrary to the protocol).

For the 72 patients with positive axillary nodes, the number of complications was greater after nodal irradiation (24% versus 10%): 3 of the 31 patients without nodal

TABLE 3. Comparison of Types of Relapse by Surgical Treatment

	Tumorectomy	Mastectomy
No. of patients	88	91
5-year local recurrence rate	5%	12%
5-year distant metastasis rate	12%	18%

The differences are not significant.

TABLE 4. Characteristics of the Patients: Second Randomization

	No nodal irradiation (n = 31)	Nodal irradiation (n = 41)
Age mean +/- SD	54.4 +/- 7.9 yr	49.5 +/- 9.6 yr
Clinical dimension of tumor mean +/- SD	18.5 +/- 5.3 mm	17.7 +/- 7.1 mm
Percent of cases with internal or medial tumor localization	32%	41%
Histologic dimension of tumor mean +/- SD	16.7 +/- 3.9 mm	16.6 +/- 3.7 mm
Percent of cases with four or more positive axillary nodes	16%	29%
Percent of cases with Bloom 3	23%	32%

Note = positive patients only.  
n: number.

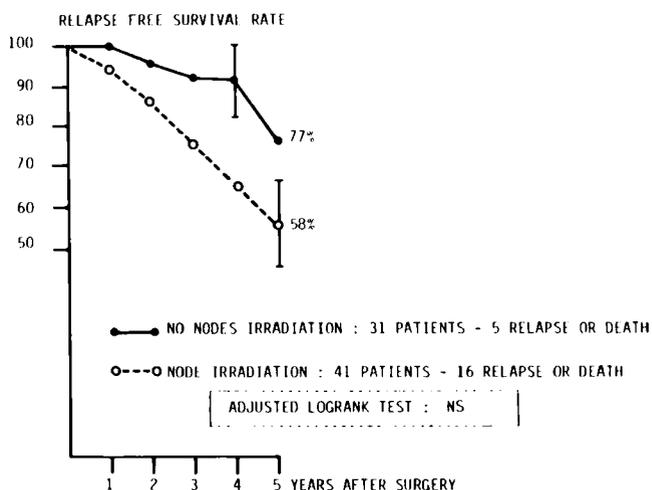


FIG. 6. Relapse-free survival by lymph node irradiation.

irradiation developed lymphedema of the arm, and 10 of the 41 irradiated patients had various complications. There were five cases lymphedema of the arm (one of these patients developed an angiosarcoma, Stewart-Treves type), one case of brachial plexus disorder, one case of respiratory disorder, and 3 cases of peri-arthritis.

### Discussion

This trial had two aims. In the first part of the trial, conservative surgery plus breast irradiation was compared with the classical mastectomy for breast cancers whose macroscopic diameter did not exceed 20 mm. Conservative surgery at the Institut Gustave-Roussy comprised: (1) simple local excision of the tumor, but neither quadrantectomy nor segmentary mastectomy, and (2) no systematic complete axillary dissection. There is no evidence that the chances of cure are worse after this conservative treatment than after mastectomy. The boost to the tumor bed in our series was given by external irradiation, and we observed an overall local recurrence rate of 5%. However, the local breast recurrence rate was only 3%, similar to that observed by Pierquin and associates<sup>5</sup> and Hellman and Harris,<sup>7</sup> who used interstitial irradiation for the boost. We think that the esthetic results are better after local excision plus external irradiation than those obtained after lumpectomy plus interstitial irradiation or after more extensive surgery. For us, lumpectomy plus external irradiation appears to be, in 1983, the best treatment for small tumors (20 mm or less). This conservative treatment might even be adequate for larger tumors (20 to 25 mm or 20 to 30 mm for instance), but this hypothesis remains to be tested.

Only patients whose extemporaneous histologic examination of axillary nodes proved to be N+ underwent complete dissection. Therefore, for the N- cases (two thirds of the cases in our study), radical axillary surgery and irradiation of the nodal areas (and consequently complications in the arm) were avoided.

In the second part of the trial, which compared post-operative irradiation of the nodal areas and nonirradiation in N+ patients, no evidence could be found in favor of nodal irradiation. The results (overall survival, disease-free survival, and metastases rates) are slightly better, and complications are less numerous in the nonirradiated group than in the irradiated group. Our irradiation technique, which includes overlapping of posterior axillary and anterior supraclavicular fields, may explain some of the complications, e.g., arm edemas and brachial plexus disorders. Now, we have abandoned this technique. Our conclusions are that if the axillary nodes are removed by surgery, the postoperative irradiation of this area is probably not necessary; patients with tumors smaller than 20 mm are very unlikely to have subclavicular positive nodes, and therefore the irradiation of the subclavicular area is

TABLE 5. Comparison of Type of Relapse According to Complementary Treatment

	No RX	RX
No. of patients	31	41
5-year local recurrence rate	15%	10%
5-year distant metastasis rate	11%	39%

The differences are not significant.  
RX: treatment.

probably useless; the usefulness of the irradiation of the internal mammary nodes is an open question. These nodes are frequently involved in patients with these small tumors (one third of the cases in a series of 111 cases treated in our center between 1954 and 1967). Moreover, a previous study in our center<sup>17</sup> showed that the patients with internal or medial tumors had longer survival after surgery or radiotherapy to the internal mammary nodes than the patients not treated in this area.

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