

Side effects following conservative therapy for a carcinoma of the breast

Initial results with Hivamat (histological variable-manual technique)

G. Schönfelder and D. Berg

**Gynecological Clinic, City of Amberg
Marienkrankenhaus,
Academic Hospital, University of
Erlangen-Nürnberg
(Director: Prof. D. Berg)**

Conservative breast carcinoma therapy recommended at present only with postoperative irradiation - side effects entailed: fibroses, sensitivity disturbances, skin alterations, edema, restrictions of movement - Hivamat, due to improved flow equilibrium, largely prevents local edemas and pain - special form of manual lymph drainage - can be used postoperatively at once - own results good

Introduction

Conservative treatment, paying strict attention to the indications and contra- indications, occupies a firm place in today's breast carcinoma therapy procedures. Numerous prospective and retrospective studies show that the overall rate of survival and the rate of recurrence-free survival for mastectomy patients and those patients submitting to conservative treatment are essentially identical, provided that similar tumor stages are compared (12, 16, 20, 22, 29, 33, 38, 39, 42).

The goal of conservative treatment is, in addition to permitting a reliable locoregional control, to produce an optimal cosmetic result with as few side effects as possible, as well as greatly reducing the physical and psychological stress to the patient, thus ensuring a high quality of life.

Conservative procedures are today generally combined operative-radiological therapies (6, 11, 12, 20, 36). It is precisely with these patients that Hivamat most clearly demonstrates its capabilities, because - along with the trauma of operation - the skin and also the remaining breast tissue become damaged in addition, due to postoperative interstitial and/or percutaneous radiation.

Until now, manual lymph drainage has been utilized in order to eliminate one of the consequences of an operation and/or irradiation, namely the lymphedema, as soon as it appears: in some cases as much as 1 to 2 years after treatment

Our development of a special form of manual lymph drainage ("Hivamat") has made it possible to begin using this procedure prophylactically from the first day postoperative, in an attempt to prevent the formation of a lymphedema as can be expected at a later point in time, through a sufficiently early rechanneling of the lymph drainage paths. To our surprise, the technique has also proved to be successful in inhibiting the occurrence of other typical side effects usually incurred following treatment.

The present study presents initial results concerning the side effects following conservative therapy and optimization of therapy in regard to reducing side effects in those patients treated with Hivamat.

Patient population and method

At the gynecological clinic in Amberg, since November 1987 the side effects and psychic states observed during postoperative stationary tumor control and during special consulting hours devoted to the cosmetic aspects of surgery in patients having undergone a breast carcinoma operation were evaluated. All patients were assessed by the same physician, in most cases several times at intervals of 6 months.

Of particular importance to the study was the documentation of the following clinical criteria:

1. consistency of operated and irradiated breast compared with other side
2. pain, disturbances in sensitivity of the breast treated
3. skin alterations (hyperpigmentation, depigmentation, edema, erythrodermia, telangiectases, desquamation, lysis, necrosis, etc.
4. arm mobility and fine motor response
5. pain, paresthesias, sensation of tenseness in the arm or axilla of the operated side
6. lymphedema (as revealed by three-point measurement, compared with other side)

The Hivamat (histologically variable manual lymph drainage technique) intensification system decidedly enhances the effectiveness and lasting benefit of the known manual massage techniques.

The unit was developed by Seidel and Waldner, specialists for massage treatment in the physical therapy department of the City of Amberg Marienkrankenhaus. It has been used in surgery, urology, pediatrics, internal medicine, ENT and gynecology, as well for the entire outpatient postoperative control examinations at our hospital for several years.

Physical principle

A strong, pulsating electrostatic field is built up between the hands of the attending therapist and the body of the patient, which becomes effective during the massage. The hands determine the pressure applied to the tissue, controlling and defining the course of the procedure. A pervasive vibrational and pumping effect arises, penetrating deeply into the tissue. This greatly intensifies the effectiveness of classical massage techniques, as well as those of connective tissue massage and manual lymph drainage.

The maximum voltage applied is 500 Volts, while the current strength is in the microampere region. Both the therapist and the patient are connected to the Hivamat, to be viewed as a voltage source with high internal resistance, much as for high-voltage therapy. Frequencies of 5-50 Hz, amplitude and 1: 5, 1:1 and 5:1 pulse lengths can be varied according to indication. During the treatment time, the contact surfaces are insulated with vinyl gloves; the insulation is to be viewed as a weakly conducting capacitor surface. The functional principle is based on the Johnson-Rahbeck effect and Coulomb's law, both known from physics. Active discharging in the unit ensures that no static charge buildup occurs which could discharge through the therapist or the patient.

Since February, 1988, patients submitting to conservative treatment have been given Hivamat therapy beginning on the first day postoperative. During the first 15 days postoperative, this was repeated daily except on weekends. Thereafter, the therapy was continued 2-3 times per week throughout the period of ⁶⁰Co irradiation. On the 10th day postoperative, as well as following the completion of percutaneous irradiation, however not later than 6 months after primary therapy, the patients were assessed according to the criteria outlined above. By October 1990, 56 patients undergoing conservative breast carcinoma surgery and treated with Hivamat had been evaluated. The results are compared (Table 1) with those found for a control group (n = 48).

By contrast with QUART (Veronesi), LAITT means:

- L = lumpectomy
- Λ = axillary dissection (level 1-111 over a separate L-shaped cut in the anterior axillary line
- IT = interstitial therapy (irradiation with ¹⁹²Ir with the afterloading technique, performed intraoperatively by the operator during the same anesthesia). Radiation therapy planning is carried out with our own program on a PC. The dose distribution is normalized to the isodose most nearly enclosing all needles, with the application of 20 Gy (more recently, 15 Gy).
- T = percutaneous telecobalt therapy, c. 2-3 weeks following the operation. The remainder of the breast is irradiated with opposing isocentrically tangential fields, with a dose of 42 Gy for the 80% isodose, corresponding approximately to the chest wall, in 14 sessions. The maximum skin dose is 52 Gy. The parasternal lymph nodes are irradiated alternately by a ventral, vertical stationary field with a dose of 45 Gy, calculated at a depth of 2.5 cm. Until the middle of this year, the supraclavicular region of the side operated was also irradiated with a maximum dose of 45 Gy, measured at a depth of 0.5 cm. As a result of a change in management, with a view to the practice of other tumor centers, this is now performed only in the event of a positive lymph node finding in level 111.

With the LAITT method, the tumor bed, together with the interstitial irradiation of the mamma, is then subjected to a total of at least 62 Gy, on the average about 67 Gy, compared with 47 Gy with QUART, where - when used correctly - the maximum skin dose does not exceed 52 Gy.

By comparison with an interstitial irradiation or an external booster dose at a later point in time, the advantage of this "open one-time" application is the exact knowledge of the tumor site, in turn permitting precise needle application in the tumor bed, under the tactile and visual control of the operator.

	with Hivamat	without Hivamat
LAITT QUART/segment	43 13	32 16
	56	48

Table 1
Operating technique and Hivamat treatment

Results

The results following conservative therapy are compared for patients treated with Hivamat (n = 56) and for a control group (n = 48), as shown in Figures 1-6 (as of October 1990).

The statistical significance can be calculated for all six criteria under study.

Discussion

Conservative breast carcinoma therapy is gaining increasingly in importance today (12, 16, 20, 22, 29, 33, 38-40, 42). Such techniques assume close cooperation between experienced operators, pathologists, radio-oncologists and x-ray diagnosticians. They also require assuring the patient of reliable postoperative care, which - owing to the special problems entailed (radiogenic fibroses) - cannot be delegated to inexperienced personnel.

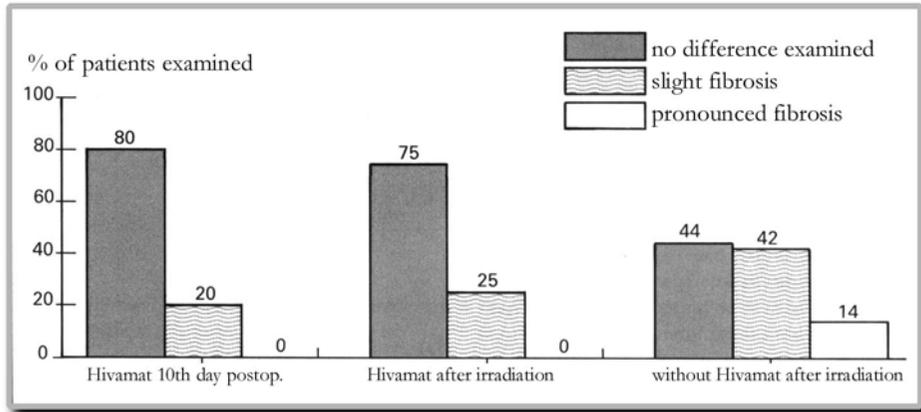


Fig. 1:

Consistency

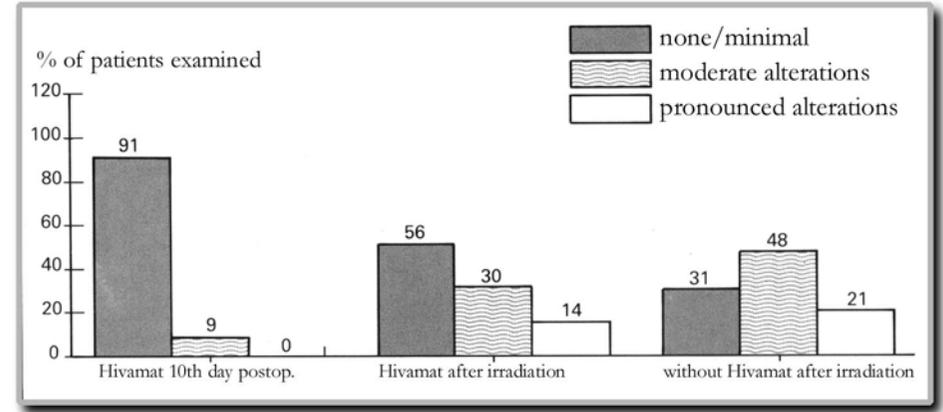


Fig. 3:

Skin alterations (hyper- and depigmentation, pasty edema, erythrodermia, telangiectases, desquamation, epithelial lysis, necrosis)

Fig. 2:

Pain and disturbances in sensitivity of the breast treated

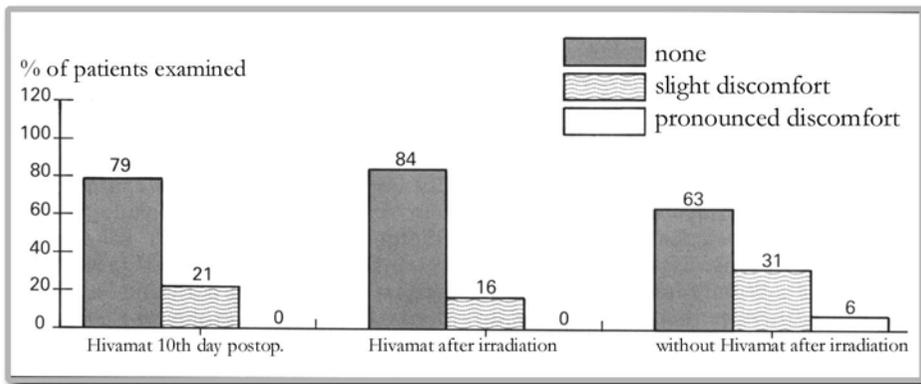
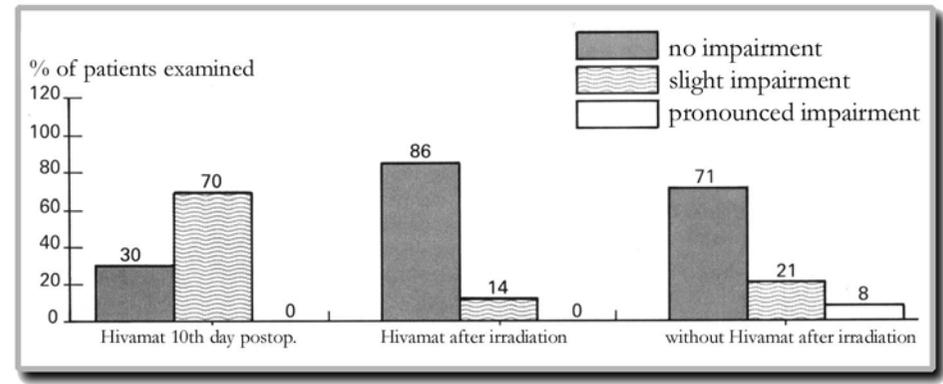


Fig. 4:

Arm mobility, fine motor response



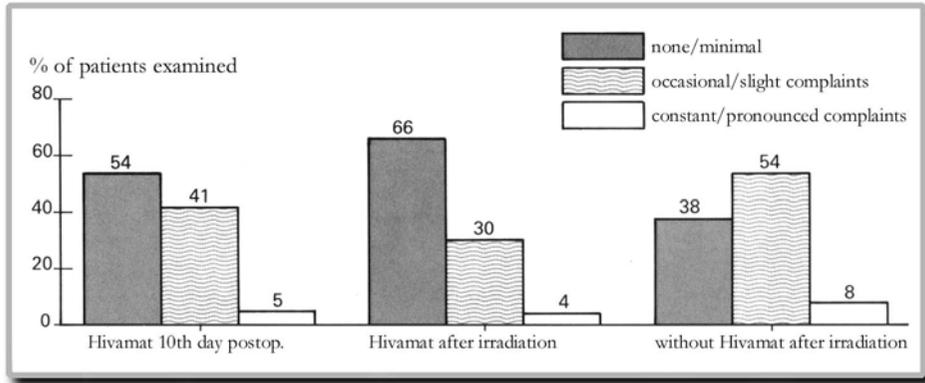


Fig. 5:

Pain and disturbances in sensitivity of arm or axilla, loss of strength

Fig. 6:

Lymphedema of the arm (as revealed by three-point measurement, compared with other side)

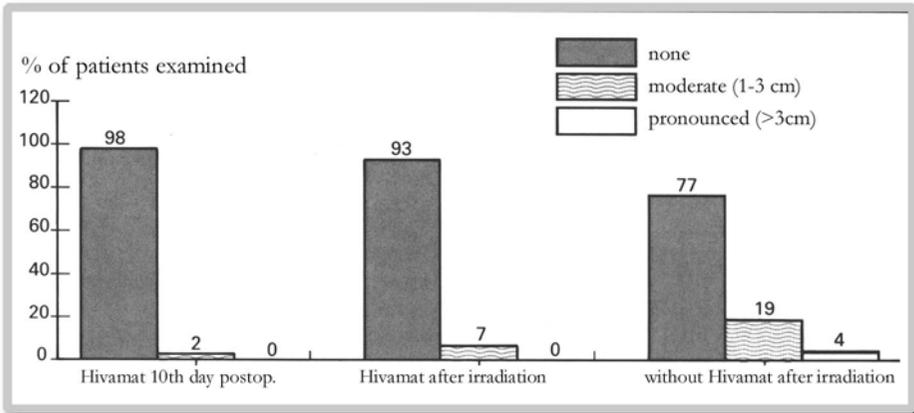


Fig. 7:

Hivamat unit and Lymph drainage technique



A postoperative irradiation serves to eliminate residual tumorous matter in the remainder of the breast and possibly in the tumor bed. At the same time, this should be done with a view to minimum morbidity. Up to now, it remains unclear how large a selective dose is necessary, whether it is possible to dispense entirely with a booster dose and, if not, how large a minimum dose is required.

It is known that doses of 45-60 Gy, applied after about five weeks, are able to sterilize subclinical tumor manifestations. Larger tumor foci require greater doses, which of course limits the recovery capacity of the tissue. It is essential to strive for a fractionation of the total dose over as many as 35 individual applications. The probability of eliminating the tumor increases with the number of fractions applied, since the probability of destroying each tumor cell in a particularly radiation-sensitive phase of the cellular growth cycle is then greater. In addition, the greater recovery capacity of the healthy tissue due to less pronounced side effects also plays an important role.

Together with the primarily cosmetic aspect, it is the therapeutical side effects which are of reatest importance for the patient's quality of life.

Engel and coworkers demonstrated an unequivocally positive correlation between the fear of recurrence and side effects of conservative treatment. Those patients without complaints had less feelings of anxiety (9).

The incidence of side effects correlates closely with the radicality of the operation (26, 46)~ Thus, for example, the formation of a lymphedema of the arm is related to the number of lymph nodes removed. The more conservative the surgical intervention, the better is the result from the cosmetic standpoint. In regard to women with small breasts, it is clear that one can hardly speak of conservative surgical intervention following a quadrantectomy or a large-scale segmental resection. Following a lumpectomy, the cosmetic-esthetic result is better, since just the tumor is cut away and thus only a narrow border of parenchyma must be sacrificed.

With more than 90% of our patients, treated according to the LAITT method, we were able to obtain a good or very good cosmetic result. This is in good agreement with the results reported by other groups (14,27,28).

The Harderand Laffergroup in Basel demonstrated the relationship between the number of lymph nodes removed and the formation of a lymphedema of the arm for postoperative irradiation of the lymph drainage paths (19). That dispensing with the postoperative irradiation of the axilla and supraclavicular region can lessen the risk of a secondary lymphedema has also been shown by Kissin (26) and Engel and coworkers (19).

The side effects following conservative therapy are, furthermore, dependent on the extent of postoperative irradiation (14). At the 2nd "Early Stage Breast Cancer" Symposium in June 1988 in New York, Vilcoq (Paris) reported on the results found with 518 patients. The limit for a good cosmetic result was a skin dose of 68 Gy. Poor results were observed with an average superficial dose of 76 Gy (44). In 1988, Habibollahi and coworkers (Guy's Hospital, London) showed that skin doses above 50 Gy are already sufficient to cause poor results (18). Similar results were presented in a talk by Harris and coworkers (Boston) in 1988 in New York, with the recommendation to reduce the irradiation dose to 45 Gy for the entire breast and not to exceed a booster dose of 16 Gy for the tumor bed. Largely on the basis of the experience of the Hunig and Walthergroup in Basel (24), as well as that of other centers (1,2,4,5,7,21,32,35,41,42), and also as a result of the recommendations made at the Consensus Conference in June 1985 in New York, we have modified our irradiation procedure to no longer irradiate the axilla and to irradiate the supraclavicular region only with pN 1 b and pN 2 patients. Centrally and medially located tumors require the additional irradiation of the parasternal lymph nodes.

On the other hand, the more restrained the surgical intervention, the more important a sufficiently intensive postoperative irradiation of the breast operated becomes. It is undeniable that adequate irradiation reduces the rate of recurrence in the breast operated. Fisher and coworkers (NSABP Study Report B-06), as well as Clark and coworkers, showed in good agreement that the local recurrence rate following conservative therapy without postoperative irradiation in an observation

center over a period of up to 10 years amounted to nearly 30%/0 (6,11).

The local recurrence rates following conservative therapy and postoperative irradiation with observations of the course of treatment covering, in some cases more than 10 years are found to lie world-wide between 4 and 14%. For the patients treated in our clinic by the LAITT method, up to now the local recurrence rate over an average observation time of 32 months (maximum 61 months) amounts to 1.4%.

Lagios and coworkers (30,31) and also Fisher (10, 11) and Bahnsen (3) were able to show that it is not possible to dispense with an irradiation even for DCIS, particularly for foci greater than 2.5 cm in diameter.

A direct comparison of the side effects found by the different groups is practically impossible, since different operating techniques were used on the breast itself and on the axilla and differences in irradiation management cannot be taken into account properly. Moreover, due to different procedures of calculation, the doses quoted cannot always be compared directly. It is also important to have more exact information about the point in time of the irradiation (the time elapsed since primary therapy or irradiation), since this represents an important parameter.

Finally, one may not forget that the evaluation of some side effects must take place more or less subjectively, unavoidably leading to some differences on the part of different authors and their different patient groups.

More or less strongly pronounced fibroses have been cited in the national and international literature with a frequency of 13-45% (9, 14, 17, 45). The most detailed study of these figures derives from Engel and coworkers. The results correlate well with our figures.

It appears to be important, to undertake countermeasures from the very beginning against a fibrosis and also against the formation of a lymphedema, since early alterations apparently can lead to serious complications

over the next 10-15 years, whereas a low rate of side effects during the early stages does not give rise to later complications (34).

Evidently, a part of later fibroses and indurations in the breast is attributable to the postoperative formation of hematomas and seromas. Frischbiere showed that, prior to radiation therapy, a mammography frequently indicates irregularly outlined compaction foci, which can be mistaken over many years for a carcinoma (15). Because of these operation- or irradiation-induced fibroses with scar tissue formation, only physicians having sufficient experience in the interpretation of such findings should perform the postoperative examinations. Indurations in the primary tumor region are frequently interpreted by inexperienced personnel as recurring tumors.

The results available until now from the treatment of patients with Hivamat indicate a marked reduction in side effects and therefore an optimal therapy by comparison with a control group comprising patients not treated with Hivamat. The difference becomes all the more apparent in view of the fact that more patients in the Hivamat group were irradiated interstitially and percutaneously than in the control group (77%/0, compared with 67% in the control group), thus with a correspondingly higher dose than in the QUART group, so that a higher incidence of side effects was to be expected.

The rate and degree of severity of radiogenic fibroses and indurations could be lowered significantly for those patients treated with Hivamat ($p < 0.001$).

Pronounced indurations were not observed, while the control group showed an incidence of 14%! Similar results were achieved with respect to the other information documented.

Poorer cosmetic results, above all in regard to side effects of the skin, are observed with patients having very large and flabby breasts. Other authors have confirmed this observation (18, 44).

In regard to side effects occurring on the skin (hyperdepigmentation, telangiectases, edema,

erythrodermia, desquamation, epithelial lysis, necrosis), various authors have observed these with a frequency of between 10 and 27%, whereby it is necessary to point out that, by contrast with our evaluation, these results were as a rule observed at a later point in time (9, 14, 17, 45).

In the study of Engel, a total of 38% complained of pain in the breast treated (9). Our figures confirm this result. 6% of those patients not treated with Hivamat complained of pronounced or constant pain and 31% of moderate or occasional pain. The Hivamat treatment reduced these figures drastically ($p < 0.025$, see Fig. 2).

Most frequently observed among our patients and also among those of Engel and coworkers (9) were various complaints and functional restrictions of the arm on the side operated. A pronounced restriction of the arm's mobility, as observed with 8% of our patients not treated with Hivamat and 4% of the patients in Engel's study, could no longer be objectified following Hivamat treatment, even on the 10th day postoperative.

With Hivamat, rapid fatigability, lessening of strength and pain in the arm could be further significantly reduced ($p < 0.025$, see Fig. 5).

In regard to the occurrence of a lymphedema of the arm, a considerable scattering of observed frequencies has been reported in the literature, ranging from 3 to 30% (8, 9, 14, 17, 25, 27, 43, 45). The very different figures cited are due to the non-uniformity of treatment procedures, different evaluation criteria and definitions, and different operating techniques (number of lymph nodes removed).

54% of all benign lymphedemas of the arm form within the first year following axillary dissection and irradiation, two thirds of these during the first half year following therapy. Radiation damage in the form of radiofibroses is the most important complicating factor in the formation of lymphedemas (23).

An adjuvant chemotherapy, according to Engel and coworkers, also leads to negative effects (9). For these reasons, one should attempt to avoid combined damage by either operating on the axilla or administering radiation therapy (26, 37). Due to the pathophysiology, the method of choice for the therapy of a lymphedema of the arm, manual lymph drainage, can be combined with compression treatment and elevation (23). Diagnosis at the earliest possible moment in time or a prophylactic insertion greatly improves the prognosis for recovery and lessens the extent of later complications, such as a fixed lymphedema or elephantiasis (13) The use of such an edema prophylaxis can also reduce the cost of treatment considerably.

At our clinic, with Hivamat we were able to lower the rate of lymphedemas from 23% (4% severe, difference in size > 3 cm/19% moderate, difference in size 1-3 cm) to 7%: Severe lymphedemas have not yet been observed after treatment with Hivamat.

Contra-indications for a Hivamat therapy are acute arm vein thrombosis and acute erysipelas.

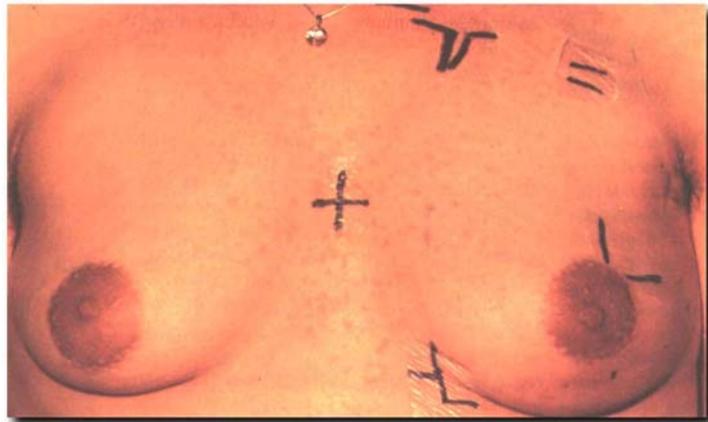


Fig. 8:

41 year-old patient; condition following LAIT, 10 days after concluding percutaneous postoperative irradiation (cobalt); treated with Hivamat



Fig. 9:

37 year-old patient; six weeks postoperative (LAIIT) and two weeks after concluding percutaneous postoperative irradiation (cobalt); treated with Hivamat

Fig. 10:

69 year-old patient; condition following LAIT, three months postoperative and nine weeks after concluding per-cutaneous postoperative irradiation (cobalt); treated with Hivamat



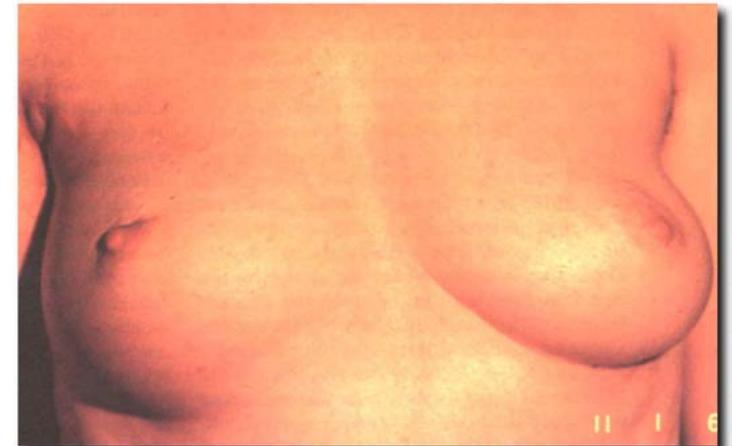
Fig. 11:

The same patient as in Fig. 10



Fig. 12:

53 year-old patient; condition following LAIT, six months postoperative and four months after concluding percutaneous postoperative irradiation; treated with Hivamat



Summary

Conservative breast carcinoma therapy is, in view of its high psychological and cosmetic advantages, to be preferred, provided that this ensures the hygienization of the tumor site. It is furthermore to be hoped that the patient does not avoid preventive examinations due to the fear of having to submit to a breast removal or even remain silent in the face of a finding resulting from self-palpation.

The significance of side effects, which together with cosmetic aspects, are of decisive importance for the quality of life of the patient should be given greater consideration today during the planning and operating phases, as well as the postoperative treatment, of conservative breast carcinoma therapy. A satisfactory cosmetic result and greatly reduced side effects are after all the very reasons for employing conservative procedures.

Typical side effects of radiation therapy following conservative breast surgery (QUART or LAITI), including axillary extirpation, are fibroses, pain or disturbances in the sensitivity of the breast operated, skin alterations (hyperpigmentation, depigmentation, edema, erythrodermia, telangiectases, desquamation, epithelial lysis, necrosis, restrictions to movement of the arm including disturbances of fine motor response, pain, paresthesias, lessening of strength in the arm on the side operated, and a lymphedema. Hivamat is used for the rapid dissimulation of local edemas, for the dissolution of indurations of the connective tissue, for improving motional readiness, and for improving the flow equilibrium and permanence of pain relief.

The treatment represents a special form of manual lymph drainage, with which an oscillating electrostatic force field builds up between the hands of the therapist and the body of the patient, giving rise to a vibrational and pumping effect which is still effective deep within the tissue. 15-20 minutes therapy daily are sufficient. Another particular feature of the Hivamat technique is that the lymph drainage can already be employed on the very first day

postoperative, in order to restore lymph drainage after this has been damaged operatively or radiologically. It is our assumption that the rate of lymphedema occurrence following a prophylactic Hivamat lymph drainage will still be lower, even after 2-3 years.

Up to now, Hivamat-supported lymph drainage has shown significant improvements in the results for the following clinical criteria, compared with conventional manual lymph drainage: consistency; pain and disturbances to the sensitivity of the breast operated; skin alterations; arm movement; pain, paresthesias in the arm and/or axilla of the side operated, and lymphedema.

Literature

1. AMALRIC, R. u. Mitarb.: Radiation therapy with or without primary limited surgery for operable breast cancer: A 20-year experience at the Marseilles Cancer Institute. *Cancer* **49**, 30 (1982).
2. AMALRIC, R. u. Mitarb.: Conservation therapy of operable breast cancer – Results at 5, 10 und 15 years in 2216 consecutive cases. In: HARRIS, J. R. u. Mitarb. (Hrsg.): *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*, S. 15. Lippincott, Philadelphia 1983.
3. BAHNSEN, J. B. u. Mitarb.: Das intraduktale Mammakarzinom. Klinische, röntgenologische und histologische Befunde und ihre therapeutischen Konsequenzen. *Geburtsh. Frauenheilk.* **34**, 488 (1985).
4. CALE, R. u. Mitarb.: Conservative management of operable breast cancer. Ten years' experience at the Foundation Curie. *Cancer* **42**, 2045 (1978).
5. CLARK, R. M. u. Mitarb.: Breast cancer: A 21-year experience with conservative surgery and radiation. *Int. J. Radiat. Oncol. Biol. Phys.* **8**, 967 (1982).
6. CLARK, R. M.: Alternatives to mastectomy – The Princess Margaret Hospital experience. In: HARRIS, J. R. u. Mitarb. (Hrsg.): *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*, S. 35. Lippincott, Philadelphia 1983.
7. DELOUCHE, G. u. F. BACHELOT: Tumoréctomie et radiothérapie pour les petits cancers du sein opérable d'emblée – résultats à 5 et 10 ans. *J. eur. Radiothér.* **1**, 563 (1980).
8. DELOUCHE, G. u. Mitarb.: Conservation treatment of early breast cancer: long term, results and complications. *Int. J. Radiat. Oncol. Biol. Phys.* **13**, 29 (1987).

9. ENGEL, K. u. Mitarb.: Zur Frage der Lebensqualität nach brusterhaltender Therapie des Mammakarzinoms. *Frauenarzt* **29**, 697 (1988).
10. FISHER, E. R. u. Mitarb.: Pathologic findings from the national surgical adjuvant breast project (protocol 6). I. Intraductal carcinoma (DCIS). *Cancer* **57**, 197 (1986).
11. FISHER, B. u. Mitarb.: Five year results from the NSABP trial comparing total mastectomy to segmental mastectomy with and without radiation in the treatment of breast cancer. *New Engl. J. Med.* **312**, 665 (1985).
12. FISHER, B. u. Mitarb.: Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *New Engl. J. Med.* **312**, 674 (1985).
13. FÖLDI, E. u. M. FÖLDI: Die Therapie chronischer Gliedmaßenödeme. *Z. Allgemeinmed.* **62**, 955 (1986).
14. v. FOURNIER, D. u. Mitarb.: Erfahrungen mit der brusterhaltenden Behandlung – Kontraindikationen, Risiken, Komplikationen. In: BOHMERT, H. (Hrsg.): *Brustkrebs*, S. 126. Thieme, Stuttgart 1989.
15. FRISCHBIER, H.-J.: Erfahrungen mit der brusterhaltenden Operation und Radiotherapie. In: BOHMERT, H. (Hrsg.): *Brustkrebs*, S. 120. Thieme, Stuttgart 1989.
16. GENZ, T.: Kritische Analyse der Brustkrebsbehandlung (1963–1982) unter Bestimmung identischer morphologischer Prognosefaktoren und besonderer Wertung der brusterhaltenden Operation. *Habil.-Schrift, Freie Universität Berlin* 1985.
17. GENZ, T. u. Th. WEYERSTAHL: 47. Kongreß der Deutschen Gesellschaft für Gynäkologie und Geburtshilfe, München 1988. *Arch. Gynaek.* **245**, 713 (1989).
18. HABIBOLLAHI, F.: Assessment of skin dose and its relation to cosmesis in the conservative treatment of early breast cancer. *Int. J. Radiat. Oncol. Biol. Phys.* **14**, 291 (1988).
19. HARDER, F. u. Mitarb.: Behandlung des kleinen Mammakarzinoms nach den Richtlinien der Basler Studie. *Chirurgische Aspekte*. In: BOHMERT, H. (Hrsg.): *Brustkrebs*, S. 104. Thieme, Stuttgart 1989.
20. HARRIS, J. R. u. Mitarb.: *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*. Lippincott, Philadelphia 1983.
21. HARRIS, J. R. u. Mitarb.: Clinical studies on the use of radiation therapy as primary treatment of early breast cancer. *Cancer* **53**, 705 (1984).
22. HERFARTH, Ch.: Diskussionsformen: Unter welchen Indikationen sind limitierte Eingriffe beim Mammakarzinom derzeit für Sie vertretbar? *Langenbecks Arch. klin. Chir.* **363**, 219 (1985).
23. HERPERTZ, U.: Armlymphödem infolge Brustkrebs. *Diagnose, Therapie und Prophylaxe. gynäkol. prax.* **12**, 507–520 (1988).
24. HÜNIG, R. u. Mitarb.: Radio-onkologische Aspekte. In: BOHMERT, H. (Hrsg.): *Brustkrebs*, S. 109. Thieme, Stuttgart 1989.
25. INGIANNI, G. u. Mitarb.: Klinische Erfahrungen in der Anwendung von lympho-venösen Anastomosen beim sekundären Lymphödem. *Handchir. Mikrochir. Plast. Chir.* **17**, 43 (1985).
26. KISSIN, M. W. u. Mitarb.: Risk of lymphedema following the treatment of breast disease. *Br. J. Surg.* **73**, 580 (1986).
27. KRISHNAN, I. u. Mitarb.: Perioperative interstitial irradiation in the conservative management of early breast cancer. *Int. J. Radiat. Oncol. Biol. Phys.* **13**, 1661 (1987).
28. KRISHNAN, I. u. Mitarb.: Cosmetic results in early breast cancer treated with lumpectomy, perioperative interstitial irradiation, and external beamradiation. *Int. J. Radiat. Oncol. Biol. Phys.* **15**, 205 (1988).
29. KUBLI, F. u. D. v. FOURNIER: *Brusterhaltende Therapie des Mammakarzinoms*. In: MELCHERT, F. u. Mitarb. (Hrsg.): *Akutelle Geburtshilfe und Gynäkologie*, S. 280. Springer, Berlin 1986.
30. LAGIOS, M. D. u. Mitarb.: Duct carcinoma in situ: Relationship of extent of noninvasive disease to the frequency of occult invasio, multicentricity, lymph node metastases and short term treatment failures. *Cancer* **50**, 1309 (1982).
31. LAGIOS, M. D. u. Mitarb.: Pagets disease of the nipple. Alternative management in cases without or with minimal extent of underlying breast carcinoma. *Cancer* **54**, 545 (1984).
32. MONTAGUE, E. D. u. Mitarb.: Conservation surgery and radiation therapy in the treatment of operable breast cancer. *Cancer* **53**, 700 (1984).
33. MONTAGUE, E. D. u. Mitarb.: Conservation surgery and irradiation as an alternative to mastectomy in the treatment of clinically favorable breast cancer. *Cancer* **54**, 2668 (1984).
34. MONTAGUE, E. D. u. M. D. McNEESE: Wirksamkeit der Strahlentherapie beim operablen Mammakarzinom. In: BOHMERT, H. (Hrsg.): *Brustkrebs*, S. 71. Thieme, Stuttgart 1989.
35. PIERQUIN, B.: Conservative treatment for carcinoma of the breast; experience of Créteil – ten year results. In: HARRIS, J. R. (Hrsg.): *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*, S. 11. Lippincott, Philadelphia 1983.
36. PROSNITZ, L. R. u. Mitarb.: Radiotherapy instead of mastectomy for breast cancer – the Yale experience. In: HARRIS, J. R. u. Mitarb. (Hrsg.): *Conservative Management of Breast Cancer. New Surgical and Radiotherapeutic Techniques*, S. 67. Lippincott, Philadelphia 1983.

- 37. SALMON:** 2. Symposium »Early Stage Breast Cancer« New York 1988. Mitt. dt. Ges. Senologie, Juni 1989, S. 4.
- 38. SARRAZIN, D. u. Mitarb.:** Conservative treatment versus mastectomy in breast cancer tumors with macroscopic diameter of 20 mm or less. *Cancer* **53**, 1209 (1984).
- 39. THOMSEN, K.:** Wandel in der Therapie des operablen Mammakarzinoms. *Fortschr. Med.* **105**, 425 (1987).
- 40. TOBIAS, J. S. u. M. J. PECKHAM:** Primary Management of Breast Cancer: Alternatives to mastectomy. Arnold, London 1985.
- 41. VERONESI, U. u. Mitarb.:** Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancer of the breast. *New Engl. J. Med.* **305**, 6 (1981).
- 42. VERONESI, U. u. Mitarb.:** Local control and survival in early breast cancer: the Milan trial. *Int. J. Radiat. Oncol. Biol. Phys.* **12**, 717 (1986).
- 43. VERONESI, U. u. Mitarb.:** Randomized trials comparing conservation techniques with conventional surgery: An overview. In: TOBIAS, J. S. u. M. J. PECKHAM (Hrsg.): Primary Management of breast Cancer: Alternatives to Mastectomy. Management of Malignant Disease Series, S. 131. Arnold, London 1985.
- 44. VILCOQ:** 2. Symposium »Early Stage Breast Cancer« New York 1988. Mitt. dt. Senologie, Juni 1989, S. 4.
- 45. WALTHER, E. u. Mitarb.:** Richtlinien der Basler Studie – Erfahrungen und Ergebnisse. In: BOHMERT, H. (Hrsg.): Brustkrebs, S. 117. Thieme, Stuttgart 1989.
- 46. YEAH, E. K. u. Mitarb.:** Primary breast cancer, complications of axillary management. *Acta radiol. oncol.* **25**, 105 (1986).

Prof. Dr. D. Berg und
Dr. G. Schönfelder
Städtisches Marienkrankenhaus
Postfach 2153
8450 Amberg