

The transmammillary approach:

Targeted treatment in breast conserving surgery

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All around the world, almost half the women with breast cancer are under threat of losing this organ. In Germany, the number of women who had to accept a mastectomy still accounted for 43% of those with the disease in 2004 (table 1).

Despite the incidence continuing to increase, the mortality of breast cancer has been falling in recent years. That is to say, breast cancer seems to be locally curable, providing that there is no systemic disease at the time of diagnosis and that primary therapy prevents any systemic spread. One undoubted fact is that the mortality of breast cancer can be reduced by early diagnosis and effective primary therapy.

The main questions that arise are:

- How are "early" diagnosis and "effective" therapy defined in the individual?
- Which "opportune" findings permit a curative local solution?
- How much systemic adjuvant therapy is necessary to optimise the therapeutic certainty of cure?

And last but not least – how can the presumed medical necessity be brought further into line with individual rationality, given that

- The breast is considered to be a symbol of womanhood
- It is important to maintain the outward appearance of the body
- Any side effects that may lead to personality changes must be avoided.

Adapting the concept

Client contact, so necessary for screening and early diagnosis, has to build up women's confidence in the value of diagnostic imaging as well as reduce their anxiety about possible therapeutic consequences. Motivating the increasing number of women under threat of breast cancer to risk-appropriate preventive behaviour has to be combined with calming their anxiety. However, in order to achieve both of these aims, we need to adapt not only the institutional approach but also the overall concept, in a tumour-specific and targeted manner, especially with respect to surgery. If we regard the early stage of breast cancer not as a disease of the entire organ but rather as a fairly steadily progressive malignant development within a functional lobular unit of the breast, then tumour-specific therapy has to include any components that are distant from the primary lesion but not yet invasive.

As well as elimination of the primary tumour, the concept of curative surgery incorporates an intraductal "blockade" running parallel to the lobular axis towards the nipple.

In the context of state-of-the-art therapeutic strategy, a "surgical" procedure means a targeted measure that largely conserves all structures worth keeping. The targeted precision, in terms of finding out the probable direction of spread in addition to identifying and locating the tumour itself, determines how well the target is met.

If we no longer want just to be running – more or less blindly – after the intraductal lesions that cannot be detected with imaging techniques, i.e. non-invasive or microinvasive lesions, then we have to approach the tumour from an area that is not yet involved, and work against the direction of spread.

Reversing the target direction

In accordance with current guidelines, the demonstration of tumour-free margins required to ensure complete (R0) surgical resection is based on a uniform tumour "front line", which ignores the reality that focal growth parallel to the lobular axis in the direction of the nipple is discontinuous.

However, R0 resection can only be achieved with certainty through the complete elimination of the tumour, including any components in the intraductal and lymphatic paths of dissemination.

Corresponding to the lobular anatomy, intraductal tumour development in the sagittal plane of the breast is almost always limited by the lactiferous duct with the nipple and by the pectoralis fascia [1]. To define the transverse plane, however, we have first to bid farewell to the idea of the lobular anatomy as well-ordered slices of cake. This plane is a variable that depends on the size and shape of the breast, as well as the topography of the tumour.

It is therefore legitimate to consider whether R0 resection would not be better achieved with certainty by a reversal in the target direction to suit the lobular anatomy and the pathophysiology of the tumour.

The study by Holland et al. [2], in which non-invasive or microinvasive lesions were found up to 4 cm distant from the edge of the tumour in 60% of all mastectomy preparations (figure 3), assumed that the tumour exhibits equidistant circular spread. This is not the case, however, as can be seen on mammography (figure 4).

The discontinuity of intraductal spread, interspersed with healthy tissue bridges that may be more than 10 mm in length [1], should therefore be a reason to redefine R0 resection as it appears in the guidelines and to reconsider the conventional surgical technique of working centrifugally from the tumour.

Transmammary resection of the tumour

The guidelines require 1 mm tumour-free margins for surgery combined with local radiotherapy, or distances of 5 mm and 10 mm from invasive and non-invasive tumour, respectively, for surgical intervention alone. In all cases, these recommendations largely overlook the fact that tumour growth towards the nipple is discontinuous.

And last but not least, the extensive intraductal component (EIC) is to be considered as an exclusion criterion for breast conserving surgery (BCS) only if the following are taken into account:

- the site of the tumour
- the intraductal spread of the tumour, which depends on the volume of the breast
- whether the tumour has been removed completely, together with the surrounding microinvasive foci.

Since a retromammary primary lesion resected using the transmammary approach will inevitably have a shorter intraductal component than a tumour situated basally, it is also clear that certainty and prognostic importance cannot, as a rule, be measured in centimetres.

The explanation for the local recurrence rate still being in double figures in most parts of the world may possibly be that the conventional centrifugal surgical procedure leaves behind non-invasive or microinvasive residues in the predominantly spherical tumour bed and in the retromammary area, which escape both surgery and radiotherapy. Without doubt, the retromammary area is extremely important in both regional and distant metastasis, as can be seen from the anatomy of the lymphatic drainage of the breast shown in figure 5 [4].

Grant et al. (1953) attributed the function of a "lymph pool" to Sappey's subareolar plexus, "into which flows all the lymph in the breast" and which forms a subcutaneous lymphatic anastomosis with the axilla [5].

Studies have shown that retromammary satellite tumours are to be expected in a third of cases. In 286 mastectomy specimens, Tulusan et al. (1993) found retromammary satellite tumours in 31% of cases where the primary lesion was situated outside the retromammary area [6].

Cunningham et al. (2006) also found a correlation between subcutaneously situated malignant tumours and the risk of axillary metastasis; this was with focal lesions located up to 6 mm below the skin [7].

Given that the radical therapeutic concept is oriented to the status of the lymph nodes, local surgical and radiological control immediately behind the areola is also of prognostic importance [8]. In this respect:

- Veronesi has for some years already tried to achieve intraoperative retromammary tumour control by transcutaneous retroareolar irradiation in addition to intracavity tumour bed irradiation [9].
- At the senology congress held in Lübeck in 2007, there were reports of hospitals where breast conserving surgery is extended to include removal of the nipple-areola complex (NAC) if an additional preoperative retroareolar punch biopsy is positive.

The retromammary area is therefore obviously recognised as a problem zone for local tumour control, but both the radiological and the surgical solutions are still to be regarded as unsatisfactory.

The transmammary approach which we have used for preference since 1998 – especially for peripherally situated tumours – offers the possibility of a segmental block resection that in-

cludes the retromammillary area but also meets the aesthetic requirements with barely visible scarring in the NAC. In this way, R0 surgical resection is achieved in the sagittal plane by including part of the nipple and fascia in the tissue removed (figure 6a), and in the transverse plane by targeted wound bed biopsies based on the radiographic appearance of the tissue specimen (figure 7).

The intraoperative radiographic findings in the tissue specimen (figure 7b), described as “shadow pathology” by Lanyi, are of great importance, as they provide almost complete correlation with postoperative histological R0 findings (Prof. P. H. Wunsch, Nuremberg) (table 2). These radiographically-targeted wound bed biopsies (figure 7c), which are mandatory in our procedure, ensure a histological R0 resection beyond the margin of resection presumed to be around the tumour itself.

It may also be the case that intraoperative biopsy confirmation of complete resection of the tumour from the conical bed, including in the transverse plane, allows a reduction in the volume of tissue resected and helps to prevent unnecessary revision resections.

Reversing the surgical path

With a conventional surgical technique, we work in a predominantly circular manner outwards from the tumour into tissue supposedly containing no cancer cells, i.e. it is possible that we reach a zone that only appears to give us an R0 resection. Reversing the direction of the surgical path, using a transmammillary approach to the tumour, may meet the requirements for targeted tumour-specific surgery to a greater extent than the conventional centrifugal technique does, especially if the tumour is situated in the periphery. Transmammillary segmental partial mastectomy is therefore not just a variant of minimally invasive access but possibly the appropriate tumour-specific surgical answer to intraductal and retromammillary lesions, targeted against the spread of tumour cells parallel to the axis.

The procedure can also be characterised in the following ways:

- It provides a safe and surgically aesthetic change in strategy to maintain the outward appearance of the body.
- It offers the possibility of breast conservation even in the case of a peripherally situated tumour in the flat, often pendulous, postmenopausal breast.
- It offers additional control of the microinvasive tumour components for optimised R0 resection.
- It is the essential surgical requirement to make the entire multimodal therapeutic concept for breast cancer less radical.

Removal of sentinel lymph nodes

The call for less radical surgery in the treatment of breast cancer also requires a targeted, tumour-specific procedure in the axilla. Preoperative scintigraphy of the lymphatics is the prerequisite for this, as it provides the surgeon with information not only about the site but also the number of all functional sentinel lymph nodes [11].

Experts in nuclear medicine no longer give peritumoural technetium-99m injections but now prefer subareolar injection, apparently making use of the retromammillary lymph pool described by Baessler, and its lymphatic anastomosis with the axilla. This is a further indication of the great prognostic importance of non-invasive or microinvasive retromammillary residues in regional spread and hence systemic metastasis [12].

Transmammillary segmental block resection – in combination with intraoperative radiographic findings in the anatomical specimen and histological confirmation – including taking wound bed biopsies and sentinel lymph nodes, gives a high degree of certainty of both local and regional R0 resection. Even though a relatively time-consuming interdisciplinary one step procedure,

if it is carried out carefully it not only precludes the necessity for revision operations but also probably reduces the extent of radical radiotherapy and chemotherapy

Given the change in direction of surgical technique, much more targeted radiotherapy should also be considered, taking the following developments into account:

- Studies using intraoperative radiotherapy (IORT) being carried out at present are based, amongst other things, on the knowledge that tumour cells left behind may be reactivated during wound healing, a phase that lasts several weeks [13].
- Conformational radiotherapy leaves the former target area in favour of any remaining microscopic foci distant from the cavity, including potentially involved lymphatic routes of dissemination.
- Intracavity radiotherapy changes the target direction from transcutaneous centripetal to centrifugal around the cavity

Intracavity radiotherapy, adapted to the conventional surgical approach, thus means a change in the radiotherapy target direction, in the sense of centrifugal irradiation of the margins of the wound cavity. However, the now identical target directions of the surgical procedure and the radiotherapy take even less account of the retromammillary tissue. This is a potential deficit in the certainty of an R0 resection, which can be overcome by the transmammillary approach.

Conclusions:

The currently recognisable fall in the mortality of breast cancer at the same time as its incidence is continuing to rise is possibly the result of improved primary treatment following earlier diagnosis of carcinoma of the breast. Opportune client contact and a synergistic therapeutic concept are prerequisites for preventing prognostically important systemic progression of the disease.

A reversal in the surgical target direction corresponding to the tumour conformation, i.e. using the transmammillary approach against the direction of tumour development, could mean a less radical interdisciplinary therapeutic concept that optimises the certainty of cure but at the same time maintains the outward appearance of the body:

- Transmammillary segmental block resection of breast cancer is possibly a new strategic approach to making the overall therapeutic concept less radical
- Targeted tumour-specific optimisation of local tumour control is a sine qua non for the reduction of highly stressful adjuvant therapy
- The transmammillary approach offers a greater reduction in anxiety to the increasing number of women under threat of or already affected by breast cancer.

References:¹

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Figures and tables

Fig. 1: Sites of ductal carcinoma in situ (DCIS), invasive ductal carcinoma, lobular carcinoma in situ (LCIS) and invasive lobular carcinoma: both ductal and lobular breast cancers show tumour growth predominantly parallel to the axis

Fig. 2: Carcinoma of the breast in a 90-year-old woman: mammographic findings of a focal lesion with a "tail" running parallel to the axis in the direction of the nipple

Fig. 3: Frequency of non-invasive and/or microinvasive malignant foci around the primary tumour (after Holland et al., 1985)

- a) 40% of tumours grow without non-invasive and/or microinvasive foci around the primary tumour
- b) 20% of tumours show non-invasive and/or microinvasive foci within 2 cm of the primary tumour
- c) 40% of tumours show non-invasive and/or microinvasive foci within 4 cm of the primary tumour

Fig. 4: Mammography: microcalcification in pathognomic triangular distribution, indicating the axis-parallel intraductal spread of tumour towards the nipple (after M.Lanyi, 2003 [3])

Fig. 5: Anatomy of the lymphatics of the breast with typical site of the sentinel lymph node (SLN)

Fig. 6 a: Transmammary segmental block resection of a breast tumour, taking part of the nipple

Fig. 6 b: Transmammary resection of the extensive intraductal component (EIC)

Fig. 6 c: Dermal nipple reconstruction following transmammary resection of a breast tumour

Fig. 6 d: Intracutaneous nipple reconstruction following transmammary resection of a breast tumour

Fig. 7 a (left): Craniocaudal mammogram: shows breast tumour with tail parallel to the axis

Fig. 7 b (right): Radiograph of tumour specimen with tail parallel to the axis

Fig. 7 c: Block resection with biopsies taken from the wound bed at 12, 3, 6 and 9 o'clock, as well as from the ventral and dorsal aspects

Fig. 8: Diagram showing target direction of intraoperative radiotherapy (IORT)

Table 1: Mastectomy rate for breast cancer in various countries	
France	28%
United Kingdom	31%
Belgium	37%
Italy	41%
Germany	43%
Switzerland	47%
The Netherlands	48%
USA	56%
Spain	66%
Poland	98%
Source: J. Jassem, Presentation given during the 4th European breast Cancer Congress in Hamburg, March 2004	

Table 2: Residual tumour (R) certainty in primary unilateral trans-mammillary resections (n = 98)	
R0	95
R1	0
R2	0
Rx	3



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