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BREAST CONSERVATION - STATE OF THE ART

Dongen, J.A. van; Department of Surgery, Netherlands Cancer Institute (AvLH), Amsterdam, The Netherlands and EORTC Breast Cancer Cooperative Group

The standard breast conserving therapy (BCT) is composed of lumpectomy, axillary clearance and radiotherapy directed to the breast; radiotherapy includes a boost in the domain of the excised tumor. Local recurrence risk and cosmetic result are important when the indication for BCT is discussed.

Local recurrences are also seen after mastectomy, so only an excess in local recurrence risk might be considered to be a contra indication. It might be so that the excess risk for local recurrence after BCT is specifically seen in certain subgroups of patients. Only randomized studies may provide us with hard data to outline such groups of risk.

The excess of local recurrence risk should be substantial to exclude patients for BCT. The age of the patient, the expected interval between primary treatment and the recurrence and the possibilities of cure after salvage are additional factors to consider when refining contra indications based upon local recurrence risk. There are indications that survival after salvage treatment of recurrence after BCT is not much better than after salvage treatment of recurrence after mastectomy. The treatment results of "new tumors" (i.e. late "recurrences") might be not so bad.

Cosmesis is not only influenced by extent of the surgery in relation to size of the breast but also to radiotherapy dose. Contrary to general feelings large excisions in small, flat breasts are giving better results than in big breasts where asymmetry usually is more apparent. Reduction of the other breast might be helpful.

There is great variation in the use of BCT in different countries and in different centers. Also in centers favoring BCT still 45% of the breast cancer cases are not amenable to BCT and should be treated with mastectomy. This number might be less in screened populations.

In multi-variate analysis age, completeness of excision and vascular invasion are prognosticators for breast recurrence. In uni-variate analysis extensive intra-ductal component (EIC) also is very important; EIC usually is very extensive and complete excision rarely possible.

In cases with breast recurrence, breast ablation is indicated. Basically no second BCT is possible.

Technique variations now under study include the dose of the RT boost, possibility of giving high dose irradiation after lumpectomy by brachytherapy in the area of risk alone and outlining of subgroups of patients where no radiotherapy might be needed.

To obtain possibility for BCT in larger tumors the benefit of neo adjuvant chemotherapy is under study; also a combination of wide local excision with filling of the gap with a latissimus dorsi flap (after preoperative radiotherapy and in combination with chemotherapy) is being investigated.

In some cases breast reconstruction might be competative with BCT.

Data from EORTC 10801 study and of the Amsterdam patient group will be used as illustration.

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MOLECULAR EPIDEMIOLOGY OF CANCER

I. Cuzick, Imperial Cancer Research Fund, London, UK.

Molecular epidemiology is a vast field which, in general, encompasses any study in which laboratory measurements are made on patients and some set of controls with the goal of elucidating the causes or stages of a disease process. The field can be split up in a number of different ways, for example, by the type of assay. Biochemical assays are commonly used in dietary studies to look at cholesterol fractions, fatty acids, nitrates, vitamins and other micronutrients. Immunological methods are used to document exposure to viruses and other pathogens. Physical measurements can be used to detect heavy metals in skin, hair and nails. However, the most exciting developments relate to direct measurements of DNA damage or alteration. Two new methods have opened up the way to learn more about the carcinogenic process at a basic level while still studying human populations. One is the measurement of DNA adducts involving potential carcinogens by ^{32}P post-labelling assays. These methods allow a degree of sensitivity unattainable by biochemical or immunochemical techniques and also focus on carcinogen exposure at the DNA level, which may be quite different than ambient exposures. Another revolutionary method is the use of the polymerase chain reaction (PCR) to amplify small amounts of DNA (or RNA) to look for mutations or deletions within specific genes and to detect oncogenic viruses (e.g. human papilloma virus) in very small qualities of human tissue (e.g. cervical scrapes). An important goal is to relate a specific mutation to a characteristic exposure, as has recently been done for mutations in P53 caused by UV-irradiation in patients with skin cancer.

The use of these new methods blurs the distinction between exposure and intermediate endpoint. Some measures, such as protein adducts are more closely related to exposure, while others such as somatic mutations in a critical gene may reflect late stages in the carcinogenic process. This spectrum is reflected in the potential uses of these new techniques which extend from exposure monitoring to new methods of screening and detection of pre-cursor lesions.

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THE USE OF MARKERS IN DIAGNOSIS AND TREATMENT OF CANCER. N.EINHORN, Radiumhemmet, Stockholm, Sweden.

A tumor marker can be defined as any biological aberration that indicates the presence of a tumor. Often the sourse is tumor cells which may synthesize, express or secrete at their surface substances which can be exploited as marker molecules. Some of them are related to the origin of the tumor, and some are more unique for the specific tumor. The more specific the marker is for the tumor type the more useful it is as a marker, specially if it is related to tumor growth and development and also if it can be detected early and gives possibility to early diagnosis. Onco-development markers as CEA, AFP and carcinoplacental markers as HCG and PLAP present in tissues and the curculation of normal individuals during differentiation stage of reproductive phases, maybe used as a tumor marker in certain malignant conditions. By development of monoclonal technology several cancer associated substances have been defined although none of them are restricted only to malignant tissues.

The use of monoclonal antibody has been investigated in the field of screening, early diagnosis, differential diagnosis, monitoring, imaging and therapy. One of the more useful monoclonal antibodies is CA 125 in ovarian cancer. CA 125 has documented well its usefulness in monitoring of the disease, several studies indicate its value in differential diagnosis and experimental studies are ongoing in the field of screening, imaging and therapy. Several oncogenes and suppressor genes have been investigated as a marker for different tumors. The data are conflicting but gives the impression that oncogenes studies will be fruitful complement in the field of tumor markers.