## **FECS Clinical Research Award Lecture**

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## The implication of adequate loco-regional tumor control in breast cancer – The role of adjuvant radiotherapy

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The treatment of breast cancer remains a tough challenge in oncology. Over the past 25 years major improvements in overall survival have been obtained by adding adjuvant systemic therapy to loco-regional therapy, especially in high-risk patients. Paradoxically, in the same time period there has been a tendency towards a reduction in the aggressiveness of the loco-regional therapy. This concept has been supported also by the hypothesis that breast cancer is a systemic disease only and therefore loco-regional treatment may not affect survival. However, accumulating knowledge and theoretical considerations about the natural history of breast cancer indicate that the efficacy of the loco-regional treatment in early breast cancer in itself has an impact on survival.

Mature results from the Danish Breast Cancer trials strongly support this viewpoint. In the protocols DBCG 82b and 82c, including more than 3,000 pre- and postmenopausal high-risk breast cancer patients, post mastectomy irradiation plus adjuvant systemic therapy were compared with adjuvant systemic therapy alone. With a median follow-up of 10 years the frequency of loco-regional failure was four times higher in all patients receiving systemic treatment alone versus combined treatment. The corresponding survival figures showed a significant decrement in overall survival in patients only receiving adjuvant systemic therapy (41% versus 50%). The impact on survival was the same in all prognostic subgroups but the magnitude decreased with removal of a larger number of nodes in the axilla. No major long-term radiation related morbidity has been observed. Overall these results confirm the hypothesis that optimal loco-regional treatment is a prerequisite to obtain maximal survival in breast cancer patients. Adjuvant systemic therapy alone cannot sufficiently prevent loco-regional recurrences. Thus, continuing intensive effort to find the optimal balance among all treatment modalities is worthwhile aiming for, not only in order to obtain good cosmetic and functional results but also to achieve the best loco-regional control as well as distant disease control and thereby optimal survival.