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POSTER

The thioredoxin system is of interest in conservative breast cancer treatment

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Background: It is well established that local recurrence after conservation treatment for breast cancer occurs more frequently in younger patients (especially those aged under 40) than older ones, and the effect of age is independent and more powerful than other factors, yet the reason for this increased risk in younger patients is not known.

The thioredoxin (Trx) system represents a novel target for anticancer therapy. To evaluate the suitability of targeting the thioredoxin system in breast cancer treatment, Thioredoxin (Trx1), Thioredoxin Reductase (TrxR1), and Peroxiredoxins1 (Prx1) were stained on breast tumour tissue.

Materials and Methods: Trx1, TrxR1 and Prx1 expression were examined in a cohort of 79 early stage breast cancer patients age less than 40, who were treated with radiotherapy after wide local excision and had been followed-up for 10 years, or until death. The patients were divided into two groups, depending on whether the staining levels were above or below the median for the whole group, and this grouping was performed for each of the three thioredoxin-system molecules.

Results: No significant differences in local control rates were seen for different levels of Trx1 and Prx1, but the tumours expressing higher levels of TrxR1 had a much higher rate of local (within breast) recurrence, than those with lower levels. The ten-year recurrence rate in the former group was 36%, for the latter 8% ($p < 0.01$).

Conclusions: These findings may enable the young patients at highest risk of local recurrence to be identified at an early stage, and alternative therapeutic strategies to be considered. These might include mastectomy with reconstructive surgery, or possibly exploration of the use of quinol compounds that inhibit Trx1.

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POSTER

Helical tomotherapy for difficult cases of breast cancer with anatomic variations and challenging location

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Background: Helical tomotherapy is a new form of intensity modulated radiotherapy with an integrated megavoltage CT scanner. This work intends to analyse experience and possibilities of helical tomotherapy in the treatment of breast cancer in difficult cases of anatomic variations like a funnel chest or complex tumor locations.

Materials and Methods: Between July 2006 and March 2007 seventeen patients with breast cancer were treated with helical tomotherapy in the University Hospital of Heidelberg to a total dose of 50.4 Gy after breast conserving surgery. The reason for the use of helical tomotherapy were bilateral carcinoma ($n=6$), parasternal localization and high dose to the heart or lung in conventional planning ($n=9$) or funnel chest ($n=2$). Target coverage and sparing of organs at risk were analysed. Breathing motion was assessed using 4D-CT or surface scanning with the Vision RT system. Surface dose was measured with thermo luminescence dosimetry.

Results: The patients could be treated without severe side effects. One 54 year old patient showed a CTC II skin toxicity, the rest of the patients I. The mean dose of the ipsilateral lung was 9.6 Gy in average for all patients, the V20 Gy 10.3%. The heart received an average V20 Gy of 10.3%, the contralateral breast a mean dose of 8.6 Gy. A target coverage with an average V95% of 91.9% could be achieved. Surface dose was analysed with TLDs for every patient and was measured between 1.6 and 1.8 Gy. Mean radiation time was 13.2 minutes, mean time on table 24.4 minutes.

Conclusions: Helical tomotherapy is an excellent option for the radiation of breast cancer in difficult localisation or when anatomic variations are present. Great care has to be taken to keep the dose to the contralateral breast low. In these special cases the advantages of an optimized target coverage with improved sparing of organs at risk outweigh the increased planning and treatment time and increased low dose area of the contralateral breast and axillary and supraclavicular region compared to conventional techniques.

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POSTER

Promoting best practice in the management of breast cancer using the Cancer Specialist Library website

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Background: The Cancer Specialist Library, part of the UK National Library for Health, provides high quality cancer knowledge, in an accessible format, and aims to promote best practice in the management of breast cancer. In addition to the resources currently available, there is a growing interest and support for the development of e-learning opportunities for doctors, nurses and other health professionals in the form of one and five minute on-line learning modules. Knowledge from the Library will be utilised for such modules and this initiative will be aligned to 'Supporting best Practices in E-learning across the NHS' http://www.osha.nhs.uk/document_store/11689612182_national_e-learning_bridging_document.doc.

Methods: The Cancer Specialist Library was launched in April 2005, and is freely available to all internet users. The Library focuses primarily on the evidence from research, in particular guidance and systematic reviews. Well-performed systematic reviews provide the most reliable answers to health care questions and the Library uses a rigorous, transparent methodology to identify all relevant cancer systematic reviews (including Cochrane) published since 2000. Where available, the Library links to high quality published appraisals. To ensure collections remain current, regular monthly database 'alerts' are received when new systematic reviews are published.

Results: Information is presented in a variety of ways:

- Core information; assembled for each cancer site and organised into 'Guidelines', 'Evidence', 'References' and 'Patient Information' sections.
- Knowledge Updates and maps; collections of current, reliable, high-level evidence relating to clinical activities e.g. hormone therapy for breast cancer. 'Knowledge maps' are provided to highlight where current knowledge exists and where gaps remain.
- National Knowledge Weeks; using an expert Advisory Panel, displays best current knowledge and current issues for specific cancers during one week of the year e.g. breast cancer National Knowledge Week – October 2006

Future development of the Library will see links to other types of knowledge:

- Knowledge from the analysis of data (statistics)
- Knowledge from experience (clinicians and patients)
- Knowledge about service provision (cancer services)

Conclusion: The Cancer Specialist Library currently holds a comprehensive and easily accessible range of high quality documents relating to all aspects of the treatment and management of breast cancer. The annual National Knowledge Weeks, and the development of e-learning modules, based on best current knowledge, has the potential to be used by health professionals to support continuing professional development. This in turn will promote best practice in the management of breast cancer.

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POSTER

Boosting the tumor bed with radiotherapy in early-stage breast cancer after lumpectomy: potential role for stereotactically guided dynamic conformal arc therapy versus electron beams

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Background: To assess the potential role of stereotactically guided 6 MV dynamic conformal arc therapy (DCAT) X-ray beams (Novalis?, BrainLAB), to boost the tumor bed of patients with early-stage breast cancer after tumorectomy and to dosimetrically compare this technique with a standard electron beam boost (EBB) for different tumor sizes and locations.

Material and Methods: Planning CTs of 10 women (median age, 54 years) with early-stage breast cancer treated with adjuvant radiotherapy after lumpectomy were selected. The boost volume (tumor bed, CTV) was defined as the area of architectural distortion surrounded by surgical clips. PTV margins resulted of expanding the CTV 1.0 cm in all directions. The prescribed dose was 16 Gy in 8 fractions. The following organs at risk (OARs) were outlined: the heart, both lungs, the ipsilateral breast, and

the skin covering the ipsilateral breast (i.e., a 5 mm width segment on the breast surface). Treatment plans with EBB were performed and compared to stereotactically guided DCAT. Dose-volume histograms (DVHs) were compared in both treatment techniques. The V90(PTV) (volume of the PTV that received 90% of the prescribed dose), the V50(OARs) (volume of the OARs that received 50% of the prescribed dose), a conformity index (CI), and an inhomogeneity coefficient (IH) were calculated in both techniques. **Results:** Five tumors were located in the left breast, and five in the right one. Three were located superficially (up to 4 cm), and seven were deeply located (>4 cm). The mean CTV and PTV volume were 33.7 cc (range 6.0–79.6), and 109.2 cc (range 48.7–206.0), respectively. The mean coverage of the PTV by the 90% isodose was 94.6% for DCAT, and 92.4% for EBB. The mean minimal and maximal dose to the PTV were 13.5 Gy (range 12.8–13.9), and 17.7 Gy (range 16.0–19.9) for DCAT, and 10.2 Gy (range 8.0–13.8), and 16.8 Gy (range 16.1–17.8), for EBB. The mean V50(OARs) for DCAT and EBB were: ipsilateral breast: 215.1 cc and 239.6 cc; ipsilateral lung: 12.9 cc and 145.32 cc; skin: 23.0 cc and 31.9 cc; and heart: 0 cc and 14 cc respectively. The mean CI value was 1.28 for DCAT and 2.43 for EBB. The mean IH value was 0.30 for DCAT and 0.72 for EBB.

Conclusions: Compared with electron beams, stereotactic guided DCAT with 6 MV x-ray beams may be preferred especially for deeply located breast tumors growing close to the chest wall. A marked OARs dose-sparing effect was observed, in addition to potential improvement in cosmesis after treatment.

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POSTER

Adjuvant therapy for early stage breast cancer (EBC): distant disease-free survival (DDFS) as a predictor of overall survival (OS)

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Background: OS advantages are often difficult to demonstrate in trials evaluating treatment for EBC, as this requires long follow-up (FU) and large trials. Results are also confounded by factors such as further treatment. DFS, the primary end point in many adjuvant trials, is not a consistent predictor of OS, and lack of standard definitions renders its interpretation difficult. A better, quicker end point is needed as a surrogate for OS. Distant metastases (DM), the most common type of recurrence, are responsible for the initial peak of relapse seen at 2 years post surgery and are associated with the highest risk of death compared with locoregional and contralateral events. The sites of distant relapse also affect outcome; patients with bone metastases fare better than patients with visceral disease. As reductions in DM are likely to improve outcomes, DDFS may be a better short-term OS predictor.

Methods: The impact of common adjuvant therapies (chemotherapy [CT], tamoxifen [TAM], and aromatase inhibitors [AIs]) on DM risk and OS were examined.

Results: CT trials show that improvements in DDFS often precede subsequent improvements in OS. In NSABP B14, TAM significantly improved DDFS at 4 years and OS at 10 years. In ATAC and BIG 1–98, over half of EBC recurrences are DM, but OS differences are limited by short FU. Visceral relapse was the most common site of distant relapse in BIG 1–98. Letrozole therapy significantly reduced DM risk, resulting in fewer soft tissue, bone, and visceral metastases when compared with TAM. ATAC showed no significant reduction in DM risk with anastrozole in hormone receptor-positive patients. The reason for this difference is unclear. The IES initially showed a significant reduction in DM risk, but the number of events at specific sites was not reported. Upon longer FU, a borderline significant benefit in OS in the estrogen receptor-positive/unknown subgroup favoring exemestane was seen.

Conclusion: Several adjuvant trials show that improvements in DDFS often precede significant improvements in OS. AIs show superiority over TAM in reducing DM risk (IES, BIG 1–98) in all sites of recurrent disease. DDFS may be a better, more achievable end point than OS for women with EBC and could hasten the development of future adjuvant breast cancer therapies.

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POSTER

Endocrine effects of adjuvant letrozole plus triptoreline versus tamoxifen plus triptoreline in premenopausal patients with early breast cancer

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Background: We are conducting a phase 3 trial (Hormonal adjuvant treatment Bone Effects – HOBEO) in patients with early breast cancer, comparing Tamoxifen (Tam), Letrozole (L) and L + Zoledronate (Z) for the effect on bone mineral density at 1 year. Postmenopausal and premenopausal patients are eligible, the latter also receiving monthly triptorelin (Tr). The aim of the present study is to describe endocrine effects of 6 months of adjuvant treatment with L plus Tr in premenopausal early breast cancer patients and to compare such effects with those of 6 months of Tam plus Tr.

Patients and Methods: Prospectively collected hormonal data were available for 81 women, of whom 30 have been assigned to receive Tam+Tr and 51 to L+Tr±Z, assuming that Z has no endocrine effects. Serum 17- β -estradiol, FSH, LH, D4-androstenedione, testosterone, dehydroepiandrosterone-sulphate, progesterone, ACTH and cortisol are measured at baseline and after 6 months of treatment. We compared, for each hormone, 6-months values between treatment groups, by applying Exact Wilcoxon-Mann-Whitney test. Differences between 6-months and baseline values have not been calculated to avoid dilution due to chemotherapy-induced postmenopausal values.

Results: There were no differences in change of plasma levels of testosterone, progesterone, ACTH, androstenedione, and dehydroepiandrosterone between the two groups. Significant differences are reported in the table (p < 0.05).

Hormone	Median value (range)		p value
	Treatment arm		
	Tam+Tr	L+Tr (±Z)	
Estradiol pg/ml	7.95 (<5–43.9)	4.9 (<5–24.5)	0.0008
FSH mUI/ml	2.65 (0.9–26.5)	10.8 (2.2–131.1)	<0.0001
LH mUI/ml	0.3 (0.1–1.2)	0.2 (0.1–0.8)	0.0005
Cortisol µg/d ^a	18.45 (4.6–30.3)	10.5 (5.3–17.9)	<0.0001

^aMedian cortisol serum levels were within normal range in both groups.

Conclusions: These data suggest that letrozole in combination with triptorelin, induces a more intense estrogen suppression also in premenopausal patients, as compared to tamoxifen. Such evidence makes reasonable the hypothesis that the higher efficacy of letrozole versus tamoxifen shown in postmenopausal patients could be confirmed also in premenopausal patients.

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POSTER

Tantalum and titanium surgical clips as fiducial markers for breast radiotherapy in a tissue equivalent phantom

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Background: Surgical clips are used to facilitate image guided 3D conformal radiotherapy for breast cancer. This study was designed to determine which clip type: medium tantalum (MTa), small tantalum (STa), medium titanium (MTi) or small titanium (STi), can best be visualised in a tissue equivalent phantom, using different imaging modalities.

Materials and Methods: The visibility of each clip type in each breast quadrant was graded by three blinded observers for BrainLAB ExacTrac floor mounted kilovoltage (kV), isocentric kV, and isocentric megavoltage (MV) imaging modalities. A three point grading system was used: "clearly visible", "some uncertainty" and "not visible". Binomial logistic regression and pairwise comparisons were used for analysis. For computed tomography (CT), the volume of artifact generated by each clip type in the phantom was determined at different slice and index thickness.

Results: MTa clips were best visualised (MTa > STa > MTi > STi, p < 0.0001). The visibility for different clip materials, sizes and locations was