2066 POSTER

Ultrasound-guided radiofrequency ablation of early breast cancer in a resection specimen: first results of a feasibility study

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Background: Over the past two decades there has been a transition towards less invasive local treatment of breast cancer, without altering survival rates. Nowadays minimally invasive techniques, such as radiofrequency ablation (RFA) are being studied as local treatment of invasive breast carcinoma. We performed ex vivo ultrasound-guided RFA of breast carcinoma lesions to determine the feasibility of this promising technique and evaluated the histological findings.
Materials and Methods: Radiofrequency ablation was performed of invasive ductal carcinoma – diagnosed by core needle biopsy – in postmenopausal women, immediately after the surgical procedure (lumpectomy or mastectomy). A needle was placed in the centre of the tumour using ultrasound guidence. Subsequently, the tumour was ablated for a period of 12 minutes. Pathologic evaluation of the specimen was performed using conventional hematoxilin-eosin (HE) staining as well as cytokeratin 8 staining and NADH diaphorase to assess cell viability.
Results: Up to now, 15 patients with an average age of 67.2 years (range 56.5−77.8) were included in this study. The mean tumour size was 12.5 mm (range 7−23). All procedures were technically successful. Pathology revealed complete cell death in 13 lesions, but viable cells were found in two lesions. In one specimen cytokeratin 8 revealed a microscopic focus of viable tissue and viable cells were found along the needle tract in another lesion. In one case the target lesion was completely destroyed, but viable DCIS was found just outside the ablated area.
Conclusions: Ultrasound-guided radiofrequency ablation can result in complete cell death in invasive breast cancer. These results support the use of RFA in the local treatment of breast carcinoma and an in vivo study has been initiated in our institution to determine the feasibility, safety and complications of this procedure.

2067 POSTER

Cost-effectiveness of extended adjuvant letrozole after five years of tamoxifen increases with treatment duration

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Background: The MA.17 study was a randomized double-blind placebo-controlled trial of 5 years of letrozole (LET) 2.5 mg/d in 5187 post-menopausal women with early breast cancer after 5 years of adjuvant tamoxifen (TAM). Ingle et al. examined the relationship between duration of treatment on MA.17 and outcomes, and found that the hazard ratios (HRs) for DFS decreased significantly over time. Previous analyses assessed the incremental cost per QALY gained (ICQ) of 5 years extended adjuvant LET. This analysis estimates the ICQ of alternative treatment durations of LET (1, 2, 3, 4, and 5 years) versus no extended adjuvant therapy in a split population of 50% node negative (NN) and positive (NP) patients.
Methods: A Markov model of the natural history of breast cancer (Karnon, 2002) was adapted to evaluate the cost-effectiveness of extendedadjuvant LET 2.5 mg/d in postmenopausal women. Data from the latest Lancet overview show that annual recurrence rates after year 5 (after 5 years TAM) are likely to be constant (4.2% NP; 1.6% NN). Event probabilities(contralateral, locoregional, or distant recurrence) were estimated using publishedresults of the MA17 trial. Effects of osteoporosis and recurrent events, and health state utilities were informed by published studies. Costs (2006 UK£) of breast-cancer care were obtained from a primary costing study in Scotland. A probabilistic sensitivity analysis was undertaken, and all outcomes were discounted at 3.5% annually.

	Total costs	Total QALYs	Mean ICQ	Lower 95% CI	Upper 95% CI
5 yrs TAM, no further hormonal therapy	£7,092	14.103			
No treatment interruption, 1 year LET	£7,947	14.153	£17,307	£6,238	£132,754
No treatment interruption, 2 years LET	£8,781	14.231	£13,187	£7,574	£46,153
No treatment interruption, 3 years LET	£9,497	14.330	£10,602	£7,231	£18,318
No treatment interruption, 4 years LET	£10,123	14.440	£9,002	£6,587	£13,614
No treatment interruption, 5 years LET	£10,710	14.542	£8,238	£6,226	£12,827

Results: The results table shows that the mean ICQ is under £20,000 for all LET durations. The gain in QALYs increases at a higher rate than total costs as therapy durations increase, which means that the ICQ decreases from £17,307 for a 1-year therapy duration to £8,238 for a 5-year duration. The upper CIs are low, other than for a 1-year duration.
Conclusions: The Ingle data show the longer the exposure to Letrozole the greater the benefit. The current study confirms the cost-effectiveness of extended adjuvant LET improves as treatment duration increases.

2068 POSTER

Incidence of amenorrhea after chemotherapy and paper of hormone therapy in the ovarian function in hormone sensitive breast cancer

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Background: Incidence of chemotherapy-induced amenorrhea (CIA) and the importance of ovarian function (OF) in hormone sensitive breast cancer, is not well defined. The objective of this study is to define the risk factors to achieve permanent amenorrhea after chemotherapy in premenopausal patients, and the impact of hormone therapy in OF.
Material and Methods: We have selected a total of 323 premenopausal patients from our center, diagnosed of hormone sensitive (ER and/or PR positive) invasive breast carcinoma, between January 1998 and June 2005. All received adjuvant or neoadjuvant chemotherapy consisting of anthracyclines with or without taxanes, or high dose chemotherapy followed by autologous bone marrow transplantation (ABMT). In second time, we analyze the kind of hormone treatment received. Date were obtained from the medical histories. We had two main objectives in this study: Incidence of CIA, according with patient's age and chemotherapy schedule; and restart of OF during hormone therapy.
Results: A total of 255 women with CIA, and 68 women with no amenorrhea, were analyzed. By groups of age: more than 45 years-old, 140 patients (95.2%) had CIA; range 40 and 45 years-old, 66 patients (71.74%) had amenorrhea; range 35−40 years old, 41 patients (61.1%); younger than 35 years-old 8 patients (36.3%), $p < 0.0001$. The relationship CIA versus chemotherapy schedule, shown that of a total of 212 patients in the anthracyclines regimens, 160 patients (75.4%) had amenorrhea, compared with the schedule with anthracyclines plus taxanes, with a total of 93 patients, with amenorrhea in 77 patientes (82.8%). The group that received high dose chemotherapy follow by ABMT (17 patients) had a 100% of amenorrhea, $p < 0.034$. On the other hand, 17 patients with hormone therapy restarted menstruation; 7 patients were receiving tamoxifen, 3 patients had finished tamoxifen treatment (2.3% vs. 1% respectively). 107 patients received aromatase inhibitors (AI), and 7 of them renewed menses (6.5%).
Conclusions: There is a direct correlation between patients' age and chemotherapy schedule combining anthracyclines and taxanes, and CIA. The restart of OF has a higher correlation with AI treatment.

2069 POSTER

Ultrasound-guided sentinel node procedure of non-palpable breast carcinoma

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Background: The sentinel node (SN) procedure has been well established for palpable breast tumors. For non-palpable tumours ultrasonography (US) can be used to guide the tracer injection. We evaluated the US guided injection technique for the SN procedure in patients with non-palpable breast tumours
Method: Two hundred consecutive patients with non-palpable breast tumours had peritumoral ^{99}Tc-nanocolloid injections using a 7.5 MHz US probe (NPT-group). In case of ultrasonographically non-visible cancers a guide wire was placed and the tracer was given using US to aim the injection at the tip of the wire. The yield of this technique was compared to the results of the SN-procedure in 850 patients with palpable tumours (PT group).
Results: SNs were identified on preoperative lymphoscintigraphy in 199 patients in the NPT group (99.5%), and in 843 of the PT group (99.2%). Parasternal SNs were visualized in 35 patients in the NPT group (17.5%) and in 154 in the PT group (18.1%). Axillary SNs were successfully retrieved in 98% of the patients in the NPT-group, and in 99% of the PT-group. Metastases were more common in the PT-group (35% vs. 23%; $P < .001$).
Conclusion: Using ultrasound to guide peritumoral tracer injection for SN procedure in non palpable breast cancers results in lymphoscintigraphic

visualization rates and surgical retrieval rates that are similar to the yield of the SN procedure in patients with palpable breast cancers.

2070 POSTER

Managing patients with invasive lobular carcinoma: Does the type of surgery matter? Do we need to extend the follow up period?

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Background: Breast conservation surgery (BCS) in patients with invasive lobular carcinoma (ILC) is still controversial due to its different clinico-pathological features. Most units report local recurrence (LR) and discharge patients after a relatively short follow up.
Aim of the study: To study the clinical outcome of patients treated for ILC after long term follow up.
Patients and Methods: 348 patients treated between 1989 and 1996 were reviewed. 113 patients were excluded (incomplete data in 91 and primary hormonal therapy in 22 patients). 235 patients were statistically analyzed.
Results: 79 patients (33.6%) had BCS (group I), which was followed by re-excision due to positive margins in 23 patients (29%), and 156 patients (66.3%) had mastectomy (group II). Compared to group II, tumours in group I were smaller (mean size17 v 37 mm, $p = 0.001$), multifocal (20 v 14 tumours, $p = 0.003$) and more positive margins (23 v 24, $p = 0.0009$). 33 patients (21%) in group II and all patients in group I had radiotherapy ($p = 0.0001$).
48 patients (20%) developed LR after a median follow up of 133 months (Range 24–196), (27 in group I and 21 in group II, $p = 0.0005$). Cox regression analysis of LR showed that the type of surgery, margins, adjuvant radiotherapy and chemotherapy affected LR ($P = 0.0005$, 0.02, 0.04 and 0.05 respectively).
The overall survival was 78.2%. Cox regression analysis showed that only the patients age affected survival ($P = 0.003$).
Conclusion: Local recurrence can be a late event in patients treated for ILC and extended follow up may be considered. Mastectomy offers a better local control.

2071 POSTER

High dose chemotherapy with marrow or stem cell transplantation versus conventional chemotherapy for breast cancer: an overview of randomized trials

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Background: A number of trials have compared high dose chemotherapy followed by bone marrow or stem cell transplantation (HDC) with conventional chemotherapy (CC) for the treatment of metastatic, as well as, high risk early breast cancer but results have been largely inconclusive. We performed a meta-analysis to estimate the risks and benefits of HDC.
Methods: We searched the MEDLINE database, the online proceedings of the American Society of Clinical Oncology and the San Antonio Breast Cancer Symposium to identify trials randomizing patients with breast cancer, to either HDC or CC. Data on breast cancer related outcomes, treatment adverse effects, and overall survival were abstracted from published reports. Pooled risk ratios (RR), or odds ratios (OR) when appropriate, and their confidence intervals were calculated. Values lower than one indicated a benefit from HDC. Continuity correction, proportional to the relative size of the opposite of the study, was used for studies with zero events in one arm. Results are presented in accordance with the QUOROM guidelines.
Results: A total of 20 studies were considered eligible: 14 evaluated HDC for high risk early breast cancer (5,598 women; HDC: 2,798, CC: 2,800) and 6 for metastatic disease (851 women; HDC: 438, CC: 413). In the adjuvant setting, HDC did not improve overall survival (RR, 1.01; 95% CI, 0.93 to 1.09) despite a small but statistically significant improvement in disease free survival (DFS; RR, 0.90; 95% CI, 0.83 to 0.98). Interestingly, the increase in DFS was limited to women with $\geqslant$10 involved axillary lymph nodes (RR, 0.89; 95% CI, 0.82 to 0.98), while women with 4−9 involved nodes did not derive any benefit (RR, 0.92; 95% CI, 0.81 to 1.06). HDC was associated with a clear increase in severe neutropenia (OR, 1.68; 95% CI, 1.26 to 2.26), febrile neutropenia (OR, 5.16; 95% CI, 1.30 to 20.45), deaths due to sepsis (OR, 6.83; 95% CI, 1.95 to 23.98), and all cause treatment mortality (OR, 4.42; 95% CI, 2.06 to 9.52). There was a trend towards an increased incidence of leukemia in patients allocated to HDC (OR, 1.91; 95% CI, 0.88 to 4.16). For metastatic disease, HDC was associated with a small, marginally non-statistically significant, improvement in overall survival (RR, 0.90; 95% CI, 0.80 to 1.01). The rates of complete response (RR, 1.50; 95% CI, 0.87 to 2.58), partial response (RR, 1.09; 95% CI, 0.93 to 1.29) and stable disease (RR, 0.82; 95% CI, 0.42 to 1.62) did not differ between treatment arms. Treatment related deaths were increased among patients with metastatic breast cancer randomized to the HDC group (OR, 3.62; 95% CI, 1.14 to 11.43).
Conclusion: Although there is some evidence supporting a limited beneficial effect of HDC for high risk early and metastatic breast cancer, such treatment is associated with an unacceptable increase in the incidence of life-threatening and fatal adverse events. An individual patient data meta-analysis could better define if certain patient subgroups derive enough benefit to justify the increased risk of HDC. For the time being, HDC cannot be advocated outside the clinical trial setting.

2072 POSTER

Comparison of breast irradiation in prone and supine position in early stage breast cancer patients

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Introduction: External beam radiotherapy for breast cancer patients is necessary after breast conserving therapy. Volume of breast tissue which needs to be irradiated is close to critical structures such as lung, heart; therefore an alternative prone position could be used to improve dose homogeneity during radiotherapy. The purpose of this study was to compare dose distribution within target and normal tissue volumes between two radiotherapy plans in prone and supine position in women with large and small breasts.
Material and Methods: 20 early breast cancer patients in clinical stage T1−2N0 were treated with breast conserving therapy and were dedicated for further radiotherapy. Planning CT was performed in a prone and supine position and two treatment plans for each patient were developed using conventional tangents technique. Dose volume histograms were produced and plans were compared with regard to dose volumes parameters.
Results: There was no difference between mean doses to the target volume (50.8 ± 0.57 Gy for supine position and 50.6 ± 0.76 Gy for prone position), but higher minimum dose in this volume was achieved in the prone position (35.5 ± 2.7 vs. 40.3 ± 2.4 Gy). The percentage of ipsilateral lung receiving 10 Gy was 16 ± 3.1% for supine position and only 9 ± 7.87% for prone position, 20 Gy (13 ± 2.8% and 4 ± 3.7% respectively). Furthermore, the maximum and mean dose to the ipsilateral lung and heart was lower in prone position compare to supine position.
Conclusion: Irradiation of patients in prone positions compared to supine positions improved dose distribution within target volume. Using plans generated in prone position we were able to reduce the dose to the organ at risk especially ipsilateral lung and heart.

2073 POSTER

Usefulness of imprint cytology and frozen section examination of the sentinel lymph node in patients with breast cancer

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Background: The accuracy of sentinel lymph node biopsy in patients with breast cancer should be both accurate and rapid, but unfortunately the false negative rate ranges between 10% and 20%. The aim of this study was to evaluate the usefulness of intraoperative imprint cytology and frozen section examination together in improving the sensitivity of sentinel lymph node procedure in patients undergoing curative surgery for primary breast cancer.
Patients and Methods: A series of 86 consecutive women (median age 53 years, range 34−70) with breast cancer confirmed by fine-needle aspiration biopsy, core biopsy or open biopsy and clinically negative nodes (T1N0) underwent sentinel lymph node procedure using a combined radioisotope and blue dye method. One or more sentinel lymph node were identified in all patients. A total of 126 axillary node were processed by both intraoperative imprint cytology and frozen section examination, and the results were compared against the final pathology.
Results: Permanent hematoxylin-eosin specimens reveled 44 (34.9%) metastasized axillary nodes, and confirmed breast cancer in all patients.