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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.

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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 QALY's 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.

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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.

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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 <sup>99</sup>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