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Localization of non palpable tumours in breast surgery: "the easy way"

P.S. Verduijn[1], Y.E.A. Van Riet[1], F. Janssen[2], J. Bosman[3], G.A.P. Nieuwenhuijzen[1], H.J.T. Rutten[1]. *[1]Catharina Ziekenhuis Eindhoven, General surgery, Eindhoven, The Netherlands; [2]Catharina Ziekenhuis Eindhoven, Radiology, Eindhoven, The Netherlands; [3]Catharina Ziekenhuis Eindhoven, Physics, Eindhoven, The Netherlands*

Background: Radio guided surgery is common practice in breast cancer surgery. In our institute the possibility of radio guided resection of non palpable lesions in the breast was explored using an iodine-125 labelled titanium seed.
Material and methods: After an extensive ex vivo study a feasibility study including 25 patients was performed. A radioactive titanium seed containing to 10 Mbq of Iodine-125 was implanted by the radiologist in the non palpable lesion one week before surgery. During surgery the lesion was excised using a gamma probe. Before and after surgery an X-ray was made respectively of the breast and the lump to check the position of the seed. Following this trial standard localization of non palpable lesions with a hook wire was abandoned in favor of the I-125 seed method.
Results: Extensive ex vivo research showed that the additional radio active dose of the I-125 seed to the patient and surgeon is negligible. The X-rays made in the feasibility study showed no dislocation of the seed after implantation. Performing a SN biopsy procedure in the same operation using Tc99 is not a problem. Using this technique didn't lengthen operation time. So far 151 patients underwent a lumpectomy using this method. Of these 45 patients had DCIS, 10 had positive margins further treated. 5 patients had a lobular carcinoma. One was multifocal and was removed with positive margins. 101 patients had a ductal carcinoma of which 12 had positive margins, 6 of the 12 were part of the feasibility study. The average T size is 1.8 cm the median lump is 6, 2 cm in diameter. These results are at least comparable to the historical group in our institute in which the hook wire was used.
Conclusions: The presented technique is unique in The Netherlands. After a successful trial of 25 procedures it is now the standard procedure for non-palpable breast lesions in our institute. We present our experience with the technique and the prospectively gathered data from 151 patients treated with this technique. Being able to localize the tumour days before the planned operation is a great benefit. Because of the accurate localization that is possible with this technique we use it during IORT procedures in breast cancer as well as in tumours eligible for neo-adjuvant systemic therapy that are located with the seed prior to this treatment.

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Maturity of data from the ATAC ('Arimidex', Tamoxifen, Alone or in Combination) trial

A.R. Bianco[1]. *On behalf of the ATAC Trialists' Group. [1]University Federico II School of Medicine, Naples, Italy*

Third-generation aromatase inhibitors (AIs) have demonstrated efficacy benefits over tamoxifen for adjuvant hormonal therapy in breast cancer and current treatment guidelines now recognise these agents as optimal adjuvant treatment. The ASCO technology assessment favoured using the AI that has been most studied in the setting most closely approximating to any individual patient's clinical circumstance, as data from all settings are not available for all agents, and it is unknown if the AIs are interchangeable in clinical practice.
Results from the Completed Treatment Analysis of the ATAC trial reinforce results of the first and updated analyses and demonstrate that anastrozole remained consistently superior to tamoxifen for both disease-free survival (DFS) and time to recurrence (TTR). The divergence in curves, which begins at 1 year, continues and increases out to 6 years, after completion of treatment. Furthermore, early improvements in DFS and TTR have translated into a benefit in time to distant recurrence. Treatment with anastrozole was associated with a lower incidence of serious adverse events and significantly fewer withdrawals from treatment compared with tamoxifen. No new safety concerns emerged with the treatment safety data virtually complete at 60 months' median treatment duration.
Data from several other ongoing trials support the use of anastrozole in the adjuvant setting: ITA, ABCSG 8/ARNO, ABCSG 6a, median follow-up 58, 28 and 60 months, respectively. Trials involving the AIs letrozole and exemestane further support the benefit of AIs over tamoxifen for the adjuvant treatment of postmenopausal women. The median follow-up in these trials was 26 months and 30 months for letrozole in the BIG 1–98 and MA-17 trials, respectively, and 37 months for exemestane in IES. AI trials collectively suggest that tamoxifen should no longer be viewed as the optimal treatment. However, when considering the choice of AI, it is important not only to consider the availability of data in the setting but also the maturity of the data. The full benefit: risk profile of anastrozole is known, and anastrozole remains the only AI with established efficacy and safety data with over 5 years' long-term follow-up in the adjuvant setting.

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Oral CMF regimen does not lead to adequate Relative Dose-Intensity (RDI) as early breast cancer (EBC) patients (pts) treatment; results from the NORA study

M.E. Cazzaniga[1], G. Mustacchi[2], P. Pronzato[3], A. De Matteis[4], F. Di Costanzo[5], L. Porcu[6], A. Bonetti[7]. *[1]Treviglio Hospital, Medical Oncology, Treviglio, Italy; [2]University of Trieste, Medical Oncology, Trieste, Italy; [3]La Spezia Hospital, Medical Oncology, La Spezia, Italy; [4]Pascale Institute, Medical Oncology, Napoli, Italy; [5]Careggi Hospital, Medical Oncology, Firenze, Italy; [6]Mario Negri Institute, Oncology Unit, Milano, Italy; [7]Legnago Hospital, Medical Oncology, Legnago, Italy*

NORA study aimed at investigating modalities of treatment and patterns of relapse in 3500 EBC pts, radically treated with surgery. CMF is one of the chemotherapy regimens used as adjuvant treatment in EBC pts, mainly in N− ones. We analyzed pathological characteristics of the pts who received this regimen, as well typology and dose-intensity of CMF schedules. The most frequent typology was iv 1, 8–28 CMF (77.3%), followed by 1–21 regimen (18.6%), while classical (oral CTX) regimen was chosen only in 3.9% of the pts.
1–21 CMF was administered in a population slightly older than the others (median age 62.3 vs 56.3 and 55.8 years for classical and iv 1–8, 28 CMF, respectively) and more frequently postmenopausal (82.8% vs 72.2% and 67.9%). On the contrary, classical CMF was preferred in comparison to the other two schedules in the case of positive axillary nodes (72.2% vs 53.8% and 62.5% for 1–21 and 1, 8–28 CMF). Principal reason for selecting CMF was tumor stage for classical and 1–21 regimens (66.7% and 33.9%, respectively), while standard guidelines have been considered for choosing 1, 8–28 CMF.
The planned treatment was completed in 85.9% of 1–21 CMF pts, holded in 15.4% of classical CMF pts and completed with timing or dose modifications in 16.9% of 1.8–28 CMF pts. The highest Relative Dose-Intensity (RDI = actually administered/planned) was observed in 1–21 regimen (C = 81.4%, M = 83.8%, F = 81%), while classical CMF presented a median dose reduction of 25% of all drugs (C = 76.3%, M = 74.6%, F = 74.6%). Median RDI of 1, 8–28 regimen was 78% for all drugs.
Despite international clinical studies indicated the oral CMF as the only one with proven efficacy in EBC adjuvant treatment, only a minority of pts are treated with this regimen and RDI data suggest that its efficacy could be compromised due the median reduction of all drugs by 25%. Even if not recommended and inefficacious, 1–21 CMF is largely used in older pts and it is the only one with adequate RDI.

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Invasive ductal carcinoma and invasive lobular carcinoma of the breast differ in response following neoadjuvant therapy with epidoxorubicin and docetaxel+G-CSF

C. Wenzel[1], D. Hussian[1], R. Bartsch[1], U. Pluschnig[1], U. Sevelda[1], G. Locker[1], M. Gnant[2], C. Zielinski[1], R. Jakesz[2], G. Steger[1]. *[1]University of Vienna, Department of Internal Medicine I/Oncology, Vienna, Austria; [2]University of Vienna, Department of Surgery, Vienna, Austria*

Background: Preoperative chemotherapy in patients with primary breast cancer treated with anthracyclines and taxanes results in high response rates, allowing breast conserving surgery in patients primarily not suitable for this procedure. Pathological responses are important prognostic parameters for progressive free and overall survival. We questioned the impact of histologic type invasive lobular carcinoma (ILC) versus invasive ductal carcinoma (IDC) on response to primary chemotherapy.
Patients and methods: 143 patients with breast cancer received preoperative chemotherapy consisted of epirubicin 75 mg/m^2 and docetaxel 75 mg/m^2 administered as a short i.v. infusion and a 1-hour infusion on day 1 of each 3-week treatment cycle. Therapy was administered in combination with granulocyte-colony stimulating factor (G-CSF) on days 3–10. Pathological complete response (pCR), biological markers, and type of surgery were compared between ILC and IDC.
Results: Out of 143 patients, 116 patients presented with IDC and 27 with ILC. Overall survival for IDC was 88% with a pCR of 22% compared to 81.5% with a pCR of 3.7% for ILC, respectively. Breast conserving surgery was performed in 79.3% of patients with IDC and in 55.6% of the patients with ILC. Patients with ILC were more frequently ER-positive (85.2% vs. 54.3%) and HER2 negativ (92.6% vs. 74.1%) than patients with IDC.
Conclusion: Our results demonstrates that breast cancer patients with ILC achieved a lower response rate, especially lower pCR rate, than patients

with IDC and therefore a lower possibility of breast conserving surgeries. The impact of these results in terms of progressive free and overall survival for patients with ILC will be presented.

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Does placement technique affect the early complications of mammosite™ brachytherapy? Magee-Womens Hospital experience

A. Soran, J. Falk, S. Beriwal, D.K.J. Keenan, M. Balkan, A. Harlak, M. Bonaventura, R. Johnson. *Magee-Womens Hospital, Surgery, Pittsburgh, USA*

Brachytherapy has been used as an alternative to whole breast radiation for adjuvant treatment of early breast cancer following breast-conserving surgery. Open cavity (time of lumpectomy) and closed cavity (ultrasound guided) techniques have been described for placement of Mammosite™-catheter to deliver accelerated partial breast brachytherapy (APBB). Herein, we retrospectively analyzed our registry data and report early complications of both techniques.

Eighty-four early stage breast cancer patients have undergone APBB since 2002. An open technique was utilized in 70 patients (mean age is 64 (range 45–89) years) and closed technique was used in 14 patients (mean age is 62 (range 49–78) years). A dose of 34 Gy was prescribed to 1 cm from the balloon surface using ^{192}Ir high-dose rate brachytherapy and was delivered in total of 10 fractions, given twice daily for 5 days. CT was used to confirm that the balloon surface was adherent to lumpectomy cavity and to measure the balloon surface to skin surface. The median minimum distance between balloon surface to skin was 1.4 (0.5 to 4.5) cm in the open technique and it was 1.8 (0.7 to 2.5) cm in the closed technique. Average skin dose was 273 cGy in the open group and it was 255 cGy in the closed group.

More than 50% of tumors were in upper outer quadrant in both groups. Average gross specimen size was 75.8 cm^3 in open group and 88.2 cm^3 in closed group. Re-excision rate prior to placement was 20% (14/70) in the open group and it was 29% (4/14) in the closed group. All patients received antibiotic treatment (7 to 10 days) during the Mammosite™ course. Median follow–up was 12 (4–40) months for open technique and 5 (3–28) months for closed technique.

Table 1: Acute complications of Mammosite™ brachytherapy

	Open technique (n = 70)	Closed technique (n = 14)
Leakage/drainage	2 (3%)	3 (21%)
Abscess	2 (3%)	
Wound infection	2 (3%)	1 (7%)
Balloon rupture	4 (6%)	1 (7%)
Acute skin toxicity grade 2	3 (4%)	1 (7%)

The incidence of persistent seroma (more than 6 months) was 31% (22/70) and aspiration was performed 13 times in 7 patients (10%; 7/70) in the open group. Because the median follow-up for closed group was 5 months it is early to reach any conclusion for persistent and symptomatic seroma differences. Forty-one patients have reached an average of 12 months follow-up since beginning our accelerated partial breast radiation therapy program. The overall cosmesis is excellent in 56% of patients, good in 37% of patients and fair 7% of patients based on the Harvard scale of assessing cosmesis. Despite the short follow-up and small sample size in the study, it seems that the Mammosite™ brachytherapy was well tolerated in patients with early stage breast cancer in both techniques, and overall cosmesis was excellent or good in 93% of patients.

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Different CMF regimens as adjuvant treatment for early breast cancer (EBC) in older patients (pts.): results from the NORA study

G. Mustacchi[1], M.E. Cazzaniga[2], P. Pronzato[3], F. Di Costanzo[4], A. De Matteis[5], L. Porcu[6], Z. Coccorullo[7]. [1]*University of Trieste, Medical Oncology, Trieste, Italy;* [2]*Treviglio Hospital, Medical Oncology, Treviglio, Italy;* [3]*La Spezia Hospital, Medical Oncology, La Spezia, Italy;* [4]*Careggi Hospital, Medical Oncology, Firenze, Italy;* [5]*Pascale Institute, Medical Oncology, Napoli, Italy;* [6]*Mario Negri Institute, Oncology Unit, Milano, Italy;* [7]*Pietra Ligure Hospital, Medical Oncology, Pietra Ligure, Italy*

NORA study aimed at investigating modalities of treatment and patterns of relapse in 3500 EBC pts, radically treated with surgery in 77 Italian Hospitals.

Overall, CMF was used in 928 pts (26.4%). We analyzed the main characteristics of the 246 pts (26% of all CMF) aged over 65 yrs (median 70, range 65–82) who received this regimen, as well typology and dose-intensity. The most frequent typology was iv 1.8–28 CMF (65.85%), followed by 1–21 regimen (30.89%), while classical (oral CTX) regimen was chosen only in 3.25% of the pts. In 68% of the cases CMF was followed by endocrine treatment (mainly tamoxifen).

Any CMF was administered mainly in Stage II tumors (70%) and in Node positive pts (56%: 1–21; 64%: 1.8–28). Curiously, 26% of the oncologists choose the 1–21 iv CMF considering it a standard guideline, as for 1.8–28 CMF. The planned treatment was suspended in 40% of classical CMF, in 5.5% of 1–21 CMF and in only 3.5% of the 1.8–28 regimen. Furthermore, treatment was modified (dose reduction or delay) in 11% (1–21) and 26% (1.8–28) of cases, mainly because of mielotoxicity. The administered median dose-intensity of all the drugs, as compared to the planned one, was reduced by 24.1% with classic regimen, by 20% with 1–21 and by 21.6% with 1.8–28 CMF. No substancial difference was noted between the different drugs.

In older breast cancer patients, CMF is widely used and in one third of cases the regimen of choice is the "1–21 iv", inspite of the lack of evidence from clinical trials. Actually drop outs for toxicity and dose-intensity reduction are similar to the better studied 1.8–28 CMF. The Classical "oral" CMF is not easy to manage in older patients.

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Local control, cosmesis and late sequelae following breast conserving therapy: influence of type of tumour bed boost and adjuvant chemotherapy

A. Budrukkar[1], R. Sarin[1], S. Shrivastava[1], D. Deshpande[2], K. Dinshaw[1]. [1]*Tata Memorial Hospital, Radiation Oncology, Mumbai, India;* [2]*Tata Memorial Hospital, Medical Physics, Mumbai, India*

Purpose: The aim of this report is to study the influence of type of tumour bed boost and adjuvant chemotherapy on local control, cosmesis and late sequelae in a large cohort of Indian women treated with Breast Conserving Therapy (BCT).

Materials and Methods: During 1980–2000, 1022 pathological stage I/II breast cancer patients (median age 43 years) underwent BCT. This consisted of wide excision, complete axillary clearance, whole breast radiotherapy (45 Gy in 25 fractions) with 6 MV photons plus tumour bed boost either with Low dose rate brachytherapy (LDR) of 15–20 Gy (n = 383), High dose rate brachytherapy (HDR) 10 Gy in single fraction (n = 153) or Electrons 15 Gy in 6 fractions (n = 460); ± systemic adjuvant therapy (SAT). Adjuvant chemotherapy (mostly CMF regimen) was given to 570 women. Median pathological tumour size was 3 cm (1–5 cm). Axillary node metastases were found in 39% women.

Results: The 5 and 10 year actuarial overall survival was 87% and 77% and disease free survival was 76% and 68% respectively. Actuarial 5 year local control rate was 91%. There were no significant differences in the local control between the 3 boost groups. Cosmesis was good or excellent in 78% women. At last follow-up, post radiation worsening of cosmesis over the pre radiotherapy score was observed in 10% women and was similar in the 3 boost groups. Late breast sequelae were observed in 25% women receiving single fraction HDR boost as compared to 13% in LDR ($p = 0.0003$) and 10% in electron group ($p = 0.00009$). In women receiving chemotherapy there was significant worsening in the cosmetic outcome ($p = 0.02$) while the local control and late breast sequelae were comparable.

Conclusion: The late breast sequelae were significantly more in women treated with single fraction HDR implants but the worsening of the post radiation cosmetic score between the 3 boost groups was comparable. Chemotherapy had an adverse impact on the cosmetic outcome but the late breast sequalae and local control rates were however comparable

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A Phase II trial of ultrasound-guided radiofrequency ablation of small invasive breast carcinomas

V. Khatri[1], J. McGahan[2], R. Ramsamooj[3], S. Griffey[4], J. Brock[2], M. Cronan[2], S. Wilkendorf[2]. [1]*University of California, Davis, Department of Surgery, Sacramento, USA;* [2]*University of California, Davis, Department of Radiology, Sacramento, USA;* [3]*University of California, Davis, Department of Pathology, Sacramento, USA;* [4]*University of California, Davis, Department of Comparative Pathology, Sacramento, USA*

Background: Local ablative therapy of breast cancer represents the next frontier in the evolution of minimally-invasive breast conservation therapy. The purpose of this Phase II trial was to determine the efficacy and safety of Radiofrequency (RF) ablation of small (⩽1.5 cm) invasive breast carcinomas.

Material and methods: Sixteen patients with core-needle biopsy-proven invasive breast cancer ⩽1.5 cm in diameter were enrolled in this trial.