Conclusions: Even after long-term follow-up no significant difference in either TDM or OS between BCT plus radiotherapy and MRM was found, confirming the safety and efficacy of the former as a treatment for breast cancers up to 5 cm.

212 Proffered paper oral

Radio-guided Occult Lesion Localisation (ROLL) Versus Wire-guided Localisation (WGL) in Breast Conserving Surgery for Non-palpable Breast Cancer (ROLL Study): a Randomised Clinical Multicenter Trial

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Background: For the management of non-palpable breast cancer, accurate pre-operative localisation is essential to achieve complete resection with acceptable cosmetic results. Radio-guided occult lesions localisation (ROLL) uses the radiotracer, injected intra-tumourally for sentinel lymph node identification, to guide surgical excision of the primary tumour. In a multicenter randomised controlled trial, we determined if ROLL is superior to the standard of care (i.e. wire guided localisation, WGL) for preoperative tumor localisation.

Methods: Women (>18 yrs.) with histologically proven non-palpable breast cancer and eligible for breast conserving treatment (BCT) with sentinel node procedure were randomised to ROLL or WGL. Patients allocated to ROLL received an intra-tumoural dose of 120 Mbq Technetium^{99} nanocolloid. Guided by a gamma detection probe, the primary tumor was surgically removed together with the sentinel node(s). In the WGL group, patients received a similar intra-tumoural or peri-aureolair dose of technetium in order to allow sentinel node biopsy. Ultrasound or mammography guided insertion of a hooked wire provided surgical guidance for excision of the primary tumour. Primary outcome measures were the proportion of complete tumour excisions (i.e. with negative margins), the proportion of patients requiring re-excision and volumes of tissue removed. Data were analyzed according to intention to treat principle.

Results: Three hundred and fourteen patients with 316 invasive breast cancers were enrolled. Complete tumour removal with negative margins was achieved in 140 (86%) patients in the ROLL group versus 134 (88%) ($p = 0.644$) patients in the WGL group. Re-excision was required in 19 (12%) of patients in the ROLL group versus 15 (10%) ($p = 0.587$) in the WGL group. The volume of the ROLL specimens was significantly larger than that of the WGL specimens (71 vs. 64 cm^3, $p = 0.017$). No differences were seen in the duration and difficulty of the radiological and surgical procedures, the success rate of the sentinel node procedure, and cosmetic outcome.

Conclusion: With this multicentre randomised controlled comparison, the first of its kind in patients with histologically proven breast cancer, we demonstrate that ROLL is not superior to WGL in terms of complete tumor excision and re-excision rates and that ROLL leads to excision of larger tissue volumes.

Thursday, 22 March 2012 15:30–17:00

CLINICAL SCIENCE SYMPOSIUM

The Management of Pre-Invasive Breast Cancer

213 Invited

Magnetic resonance imaging of DCIS and high-risk borderline lesions

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Magnetic resonance imaging (MRI) is the most relevant new imaging technique which emerged in breast cancer care in the last twenty years, opening a new window for diagnosing this disease. The base for MRI lesion detection is the ability to reveal neoangiogenes using dynamic image acquisition before/after intravenous administration of gadolinium-based contrast material. Thus, in the past years, MRI was considered highly sensitive (>90−95%) for invasive cancers but of limited value for detecting DCIS (60−70%). However, this view was determined by the fact that study populations were essentially composed of series of DCIS diagnosed with mammography thanks to the detection of clustered microcalcifications. When this bias was corrected using not only mammography as an entry criterion, MRI showed to be more sensitive than mammography for detecting DCIS (92% versus 56%), in particular when high-grade DCIS were considered (92% versus 48%). Moreover, differently from invasive cancers mainly appearing as 'mass-like' lesions, an important fraction of DCIS are detected on MRI as 'non-masslike' lesions, showing linear, ductal, segmental, regional, or focal distribution, typically non detectable without contrast material administration. Conversely, the dynamic behavior is not relevant fro DCIS, due to a high frequency of continuous increase (type 1) curve which might be falsely interpreted as benign. A peculiar mechanism explaining DCIS enhancement at MRI has been recently investigated: a third compartment for contrast material biodistribution other than the intravascular and interstitial ones, i.e. the intraductal space. This strengthens the higher importance of a high spatial resolution (<1 mm square) in comparison with temporal resolution, for contrast-enhanced state-of-the-art breast MRI. Obviously, sensitivity is depending on the reference standard. When the 5-mm sliced whole breast is used as reference standard and all small foci of DCIS are considered, either MRI or mammography show sensitivity lower than 50%. The role of MRI for preoperative evaluation of DCIS is under discussion. Even though MRI is the most sensitive technique for evaluating tumor extent, under- and overestimation are possible and high-quality research is needed to clearly establish its preoperative role. The transmission of three-dimensional data sets from the radiologist to the surgeon is one of the key steps, also taking in consideration that the woman is studied with MRI in prone position but is operated in supine position. Recent studies have also showed a potential relevant clinical application of MRI in ruling in or out malignancy in the peculiar setting of lesions of uncertain malignant potential (so-callede high-risk or borderline, B3 lesions) found at core needle biopsy under mammographic (stereotactical) or ultrasound guidance. Using the simple criterion of presence or absence of contrast enhancement, MRI shows a negative predictive value of 97% (undetecting only low-grade DCIS), allowing for a reliable exclusion of invasive cancers among high-risk lesions diagnosed at needle biopsy. In such a way, a rational use of MRI for strongly reducing the number of surgical procedures in this setting is proposed.

214 Invited

Surgery in relation to DCIS biology

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The key aim of surgery for ductal carcinoma in situ (DCIS) is to prevent ipsilateral invasive recurrence (mortality from breast cancer at 15 years is less than 1%).

The goal of surgery for DCIS is to ensure clear surgical margins of greater than 1 mm and to preserve cosmesis. Margin involvement occurs in 25-30% of DCIS undergoing breast conserving surgery leading to re-excision or mastectomy. DCIS size greater than 3cm multifocality, premenopausal status, oestrogen receptor positivity and comedo type, increases margin involvement at excision. A 12-gene Recurrence Score predicts ipsilateral recurrence, identifying a small group (10% of women) after wide local excision (WLE) with a 19% invasive and 27% overall recurrence who should potentially have mastectomy from the outset.

DCIS may be a function of cancer stem cell (CSC) activity. High grade DCIS produces more CSC and expresses more EGF family ligands. CSC are increased by endocrine treatments. In vitro and in vivo models indicate HER tyrosine kinase and NOTCH inhibitors prevent CSC formation and reduce growth.

Oestrogen receptor (ER) positive DCIS in postmenopausal women responds to preoperative endocrine manipulation with a fall in proliferation and significant pathological changes. Limited data indicate a reduction in DCIS size occurs on primary endocrine therapy which lowers the risk of margin involvement. Further studies of primary medical therapy for up to 6 months before surgery are required in ER positive DCIS.

Combining endocrine therapy and anti-CSC strategies will be potentially more effective in preventing local recurrence. Future randomised trials need to identify which DCIS lesions can avoid surgery (or radiotherapy) by primary endocrine therapy.

215 Invited

Radiotherapy in Relation to Biology

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DCIS is considered a precursor to invasive ductal carcinoma and its treatment is ultimately therapy for prevention of local recurrence (LR),