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Systemic Treatment Decision Making for Patients with Stage I and II, Hormone Receptor Positive, Her2/neu Negative Breast Cancer

X. Zhu[1], N. Graham[2], L. Paquet[3], S. Dent[2], X. Song[2]. [1]*The Ottawa Hospital, Department of Medicine, Ottawa Ontario, Canada;* [2]*The Ottawa Hospital, The Ottawa Hospital Cancer Centre, Ottawa Ontario, Canada;* [3]*Carleton University, Department of Psychology, Ottawa Ontario, Canada*

Background: Oncotype DX is a clinically validated risk stratification tool that can predict the risk of recurrence and the benefit of adjuvant chemotherapy in women with hormone receptor positive (HR+), HER2/neu negative early stage breast cancer (EBC). This tool has been available to oncologists in Ontario since April 2010 at significant cost, yet no guidelines exist regarding their use. This retrospective chart review examined the factors that were associated with use of Oncotype DX at a tertiary care cancer centre.

Materials and Methods: One hundred patients (pts) diagnosed with HR+, HER2/neu negative EBC (stage I-II), who underwent Oncotype DX testing between April 1, 2010, and June 30, 2011 were included in the study. A second control group of 100 patients with similar disease characteristics but who did not receive Oncotype DX testing were randomly selected. Data collection included demographics, tumor staging and Adjuvant! Online recurrence risk scores.

Results: Median age in the Oncotype DX group was 58 years (r: 26−77) and 63 years (r: 30−81) in the control group. The Oncotype DX group and control group had 22/15 premenopausal pts, 6/4 perimenopausal pts, and 72/81 postmenopausal pts, respectively. 55, 34, and 4 pts had T1c, T2, and T3 tumors in the Oncotype DX group, respectively, vs 42, 28, and 1 pts in the control group. 10 pts in the Oncotype DX group had tumor cells in at least one lymph node vs none in control group. 80 pts in the Oncotype DX group had greater than grade 1 histology vs 56 in control group. Adjuvant! Online median recurrence risk was higher in the Oncotype DX group [19% (r: 9−48%) with tamoxifen (TAM), 15% (r: 7−38%) with TAM plus an aromatase inhibitor (AI)] than the control group [12% (r: 8−36%) with TAM, 10% (r: 7−29%) with TAM plus an AI]. The mean 10-year recurrence risk in the Oncotype DX group was 20% with TAM and 16% with TAM plus AI, vs 15% and 12% in the control group, respectively. Median Oncotype DX recurrence score was 17 (r: 0−70), with 10-year recurrence risk of 11% (r: 3−34%). Further statistical analysis will be performed.

Conclusions: This single-centre series is aimed at identifying potential clinical and pathological factors which can influence physicians' decision to request Oncotype DX testing for pts with EBC. These results will be used to design a prospective study evaluating these factors and how Oncotype Dx testing may influence treatment decision making.

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A Diagnostic Genetic Test for the Physical Mapping of Germline Rearrangements in the Susceptibility Breast Cancer Genes BRCA1 and BRCA2

M. Ceppi[1], K. Cheeseman[1], E. Rouleau[2], A. Thomas[1], A. Briaux[2], C. Lefol[2], P. Walrafen[1], A. Bensimon[1], E. Conseiller[1], R. Lidereau[2]. [1]*Genomic Vision, Research & Products Development, Bagneux/Paris, France;* [2]*Hôpital René Huguenin − Institut Curie, Laboratoire d'Oncogénétique, Saint-Cloud, France*

Background: the *BRCA1* and *BRCA2* genes are involved in breast and ovarian cancer susceptibility. About 2% to 4% of breast cancer patients with a positive family history who are negative for *BRCA1* and *BRCA2* point mutations can be expected to carry large genomic alterations (deletion or duplication) in one of the two genes, and especially *BRCA1*. However, large rearrangements are missed by direct sequencing. Molecular Combing is a powerful FISH-based technique for direct visualization of single DNA molecules, allowing the entire genome to be examined at high resolution in a single analysis. We have developed a novel predictive genetic test based on Molecular Combing. For that purpose, we designed specific *BRCA1* and *BRCA2* 'Genomic Morse Codes' (GMC), also covering the non-coding regions and including large genomic portions flanking both genes.

Material and Methods: high-resolution *BRCA1* and *BRCA2* Genomic Morse Codes (GMCs) have been designed. A GMC is a series of 'dots or dashes' (DNA probes with specific sizes and colors) and 'gaps' (uncolored regions located between the DNA probes), designed to physically map and define with a specific 'signature' a particular genomic region. For the *BRCA1* and *BRCA2* GMC design, all repetitive sequences were eliminated from the DNA probes, thus reducing background noise and permitting robust measurement of the color signal lengths within the two GMCs. Both GMCs were statistically validated on samples from 10 healthy controls and then tested on 10 breast cancer patients with a positive family history of breast cancer.

Results: large rearrangements, corresponding to deletions and duplications of one or several exons and with sizes ranging from 3 kb to 40 kb, were detected on both genes, including the characterization of 4 new mutations (for *BRCA1*: Del ex 3, Del ex 24 and Dup ex 5−7; for *BRCA2*: Dup ex 17−20). The nature of the identified large rearrangements was confirmed by high-resolution zoom-in aCGH (11 k) in the same patients, and the exact breakpoints of the new mutations characterized. Importantly, the developed GMC allowed to unambiguously localize several tandem repeat duplications on both genes, and to precisely map large rearrangements in the problematic Alu-rich 5′-region of *BRCA1*.

Conclusions: we propose the developed Molecular Combing genetic test as a valuable tool for the screening of large rearrangements in *BRCA1* and *BRCA2*, to be combined in clinical settings with an essay that allows the detection of point mutations.

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Tumor to Breast Volume Ratio as Measured On MRI: a Possible Predictor of Breast Conservation Surgery Versus Mastectomy

D. Barsuk[1], R. Faermann[2], S. Schneebaum[1], F. Sperber[2]. [1]*Tel Aviv Sourasky Medical Center, Breast Health Center, Tel Aviv, Israel;* [2]*Tel Aviv Sourasky Medical Center, Department of Radiology, Tel Aviv, Israel*

Purpose: The surgical approach to breast cancer has changed dramatically in the past 20 years. Nowadays the surgical objective is to remove the tumor with negative margins and good cosmetic results. MRI of the breast has become an important imaging tool before surgery, proving to diagnose additional tumors, and to assess the tumor extent. Tumor to breast volume ratio is an important predictor of breast conservation, but was never accurately measured. MRI enables this ratio to be measured. Our purpose was to measure this ratio and to analyze if it can help in the planning of breast cancer surgery.

Materials and Methods: We conducted a retrospective hospital based study of 76 consecutive patients diagnosed with breast cancer that underwent pre-surgery breast MRI between January 2008 and September 2010 at our hospital. The volume measurements were made using a semi-automated method. The breast volume was calculated in the AW workstation. The tumor volume was calculated with CAD (Computer-Aided Diagnosis) software and the AW workstation. The tumor volume was calculated including 10 mm margins. Afterwards the ratio between the volumes was calculated.

Results: 76 patients were included in our study. 64 patients had breast conserving surgery and 12 patients underwent mastectomy. Average tumor volume in the mastectomy group was much larger than in the lumpectomy group ($p < 0.0001$). Average tumor to breast volume ratio in the mastectomy group was 0.30 (30%). In the lumpectomy group, average tumor to breast volume ratio was 0.06 (6%) ($p < 0.0001$).

Conclusion: Tumor to breast volume ratio as measured on MRI is an accurate measuring tool that can help the surgeon in the decision weather to perform breast conserving surgery or mastectomy. This tool should be introduced in the surgical planning of patients diagnosed with breast cancer.

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An Early Experience with SNOLL in the Management of Impalpable Breast Cancer

M. Galea[1], H.S.J. Ramesh[1], L.S. Chagla[1], A. Ray[1], J. Herbert[2], O. Harris[3], S. Desmond[3], R. Thind[3], R.A. Audisio[4]. [1]*St Helens and Knowsley NHS Trust, Surgery, Prescot Liverpool, United Kingdom;* [2]*St Helens and Knowsley NHS Trust, Nuclear Medicine, Prescot Liverpool, United Kingdom;* [3]*St Helens and Knowsley NHS Trust, Radiology, Prescot Liverpool, United Kingdom;* [4]*St Helens and Knowsley NHS Trust, Surgery/University of Liverpool, Prescot Liverpool, United Kingdom*

Background: The detection of impalpable breast cancer lesions is on the rise due to mass population screening. Radio-guided occult lesion localisation (ROLL) has recently been used in the management of early lesions while sentinel lymph node biopsy (SLNB) has been used to detect occult lymph node metastases. In order to optimise localisation many international centres have proposed a technique involving the combined use of ROLL and SLNB, also known as SNOLL.

Materials and Methods: All patients with impalpable invasive cancer and clinically negative axillae were analysed. The impalpable breast lesions were localised with an intra-lesion injection of 0.1 mls of 99Tc nanocolloid (1 MBq) 1 to 4 hours before surgery. SLNB was identified using 0.2 mls of 99Tc nanocolloid (20 MBq) injected subdermally in the periareolar region within the index quadrant, the day before surgery. All lymph nodes and target tissue that were focally radioactive were denoted using signals from a gamma probe.