O-56 Quality assurance issues in breast cancer pathology: a New Zealand teaching hospital experience

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This presentation looks at aspects of breast cancer pathology in the context of aiming to deliver a quality service in a public sector hospital in New Zealand. The quality assurance processes in place and the evidence for them will be discussed and reviewed. An in house HER2 testing audit will also be included and will be discussed with reference to Australasian data.

O-57 An image of cell permeability

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Water molecules are found in different environments in the body such as inside or outside the cells. When trapped inside they can only move within the cells, which make them appear to move slower than water molecules outside the cells. Therefore they have different diffusion coefficients and can be distinguished by a Nuclear Magnetic Resonance (NMR) diffusion measurement.
Our method can be used to determine the time it takes for a molecule to move from the inside of a cell to the outside and vice versa. This is called the exchange time. The exchange time is related to the permeability of the cell.
Our method is the only known non-invasive method to measure the exchange/permeability of molecules through the cell membrane on the timescale for an MRI experiment. The method offers a new way to achieve increased MRI contrast in systems where the studied molecule is not diffusing in the same way throughout the sample, i.e. where the exchange times between intra- and extra cellular compartments are different. It is reasonable to believe that the cell permeability can be correlated to different pathological conditions. Hence, it could be used as a diagnostic tool for a variety of diseases or disorders such as infarct, stroke and tumours.
Experiments have been preformed on breast cells and breast cancer cells. The results show that the method can be applied on the cells of primary interest, human breast cancer cells. Moreover we have identified a significant difference in permeability between normal and cancerous cells.
Future studies will be directed towards tissue samples and in vivo tests on rats. We will also explore the possibility to differentiate between cancer stem cells and cancer cells.

O-58 The UK MARIBS study of MRI breast screening: progress on genetic and density projects

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The MARIBS magnetic resonance imaging (MRI) study compared MRI with X-ray mammography for screening women at high risk of developing breast cancer due to a genetic disposition. This results led to revised NICE Guidelines for management of this group. Continuing studies are documenting the detailed genetic background and family history of the study cohort, and relating these to imaging features such as mammographic density, recall rates and diagnostic pathways. An audit of the family history pedigrees has been performed manually. 692 pedigrees have been collated and all but 18 have been assessed to evaluate study eligibility. There were 140 BRCA1, 70 BRCA2 and 15 TP53 positive or at 50% risk of carrying a mutation in an affected family. There were 442 with a family history of breast or breast and ovarian cancer, and 25 with Li-Fraumini syndrome. All of those from families with a known mutation met the eligibility criteria, 91% of family history and 48% of Li–Fraumini syndrome individuals were eligible. Currently 463 blood samples are undergoing whole gene sequencing. A new method of measuring breast density based on 3D MRI images has been developed. This has been piloted on 61 images from MARIBS and shown to correlate with visual scoring on a 21 point scale ($r = 0.84$, $p = 0.001$) of X-ray mammograms, and with an interactive computer analysis (CUMULUS) of the same mammograms ($r = 0.78$, $p < 0.0001$). This may provide a helpful method of refining breast cancer risk.

O-59 Identification of sub-classes of breast cancer through consensus derived from automated clustering methods

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Gene expression profiling has identified five biologically relevant breast cancer subtypes. A comprehensive definition of these subtypes using simple robust techniques, applicable to routine clinical use, remains to be determined.
We have applied different clustering techniques on protein expression to refine breast cancer subtype characterisation. Five algorithms were used for cluster analysis (Hierarchical, K-means, Partitioning Around Medoids, Adaptive Resonance Theory and Fuzzy C-means) on immunohistochemical scores of 25 proteins determined in primary operable invasive breast carcinoma ($n = 1,076$) prepared as tissue microarray. Conventional statistical techniques were used to derive characteristic biomarkers in each class. Associations between classes and clinical and pathological factors were examined.
A consensus of six distinct classes of breast cancer was determined between clustering techniques. Classes 1 ($n = 202$), 2 ($n = 153$) and 6 ($n = 80$) were characterised by high expression of luminal cytokeratins (ck7/8, ck18, ck19) and ER. Class 1 tumours expressed high levels of c-erbB-3/4, whereas Class 2 over-expressed BRCA1. Whilst Class 1 and 2 had high levels of PgR expression, Class 6 tumours had relatively low PgR expression. Class 3 tumours ($n = 77$) were characterised by c-erbB-2 over expression. Classes 4 ($n = 82$) and 5 ($n = 69$) showed basal cytokeratin expression (Ck14 and ck5/6) but were differentiated by p53. Kaplan-Meier survival analysis showed differences in survival of these groups where Classes 2 and 6 had the best overall survival, whilst Class 3 had the poorest.
In conclusion, we propose there are six biologically and clinically relevant breast cancer subtypes defined using a small panel of proteins determined using simple immunohistochemical techniques.

O-60 The role of primary stromal cell-derived chemokines in the breast tumour microenvironment

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Introduction: It is well established that within the breast tumour microenvironment, neoplastic epithelial cells coexist with stromal fibroblasts. Stromal cells secrete