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A Novel Polyhedral Oligomeric Silsesquioxane Coated Quantum Dot for Her-2 Localisation and Cancer Therapy

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Background: Quantum Dots (QDs) are fluorescent semiconductor nanocrystals that can replace the traditional fluorophores for various biomedical applications including cancer localisation, sentinel lymph node biopsy, detection of micrometastasis, image guided targeted drug delivery for chemotherapeutic agents and Photodynamic Therapy (PDT). QD technology forms one of the most promising frontiers in personalised medicine that would allow the diagnosis and treatment of disease at a truly molecular and cellular level. Their main limitation is toxicity, as most QDs are based on chalcogenide salts. We have synthesized and characterized a novel Polyhedral Oligomeric Silsesquioxane (POSS) coated QD using Mercaptosuccinic acid (MSA) and D-cysteine (D-cys) as stabilising agents and demonstrated its enhanced properties in an in vitro set up. POSS coated QDs were then conjugated to anti-Her-2 antibody and successfully used to localise Her-2 receptors on SKBR3 cells.

Materials and Methods: QDs were synthesized using POSS/MSA/D-cys (POSS-QDs) or MSA/D-cys (MSA-QDs) by a one pot aqueous method. Characterization was performed using Transmission Electron Microscopy, Fourier Transform Infrared Spectroscopy and Photoluminescence studies. In vitro cytotoxicity was assessed using Hep G2 cells and compared to toxicity of ionised Cadmium and Tellurium salts. Photostability was assessed using prolonged excitation to high UV radiation for 2 hours. Confocal microscopy was used for QD localisation in vitro. POSS QDs were conjugated to mouse anti-Her2 antibody using carbodiimide chemistry and exposed to SKBR3 (Her-2 over expressing) and MCF-7 (Her-2 under expressing) breast cancer cells.

Results: POSS-QDs had a size range of 3–4 nm and demonstrated enhanced colloidal stability and photostability (p-value <0.05) compared to MSA-QDs that became unstable on prolonged standing. FTIR confirmed the attachment of POSS to the CdTe core. Both QDs showed significantly reduced toxicity compared to ionised cadmium and tellurium (p-value <0.01). Confocal microscopy demonstrated enhanced intracellular uptake and photoluminescence of POSS-QDs at both 1 and 24 hours compared to MSA-QDs. POSS-QDs were significantly more photostable than MSA-QDs. Anti-Her-2 antibody conjugated POSS-QDs successfully localised Her-2 receptors on SKBR3 cells.

Conclusion: A POSS coating confers photostability and colloidal stability while retaining the small size and unique photophysical properties of the QDs. The amphiphilic nature of the POSS coating allows rapid intracellular uptake with enhanced photoluminescence allowing lower concentrations of QDs to be used for an overall reduced toxicity for various applications including Her-2 localisation and targeted cancer therapy.

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Is Triple Assessment Necessary in All Young Patients Referred to a Rapid Diagnosis Breast Clinic?

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Introduction: A palpable lesion in the breast is usually subjected to triple assessment: clinical examination (CE), imaging, and core biopsy (CB) or FNAC. This minimises the risk of a breast cancer being missed. However, breast cancer is rare in young women and triple assessment, especially CB, is expensive. We reviewed our experience to see whether triple assessment is necessary in young women aged less than 25 years.

Materials and Methods: We extracted and analysed the data from a prospectively entered database on women aged <25 years who attended a rapid diagnosis breast clinic over a 6-year period.

Results: Among 10,301 patients seen during the study period 972 (9.4%) were aged <25. Thirteen were men. Among others commonest presentations were suspected lump (n=776), pain (n=185) and nipple discharge (n=44). All had CE which was normal or benign in most (n=955) but indeterminate in 17. Two of these were skin lesions only over the breast. 698 (72%) also had an US which was normal (n=290) or benign (n=387) in all except in 21 patients in whom it was indeterminate. In 6 patients both were indeterminate. Three hundred and thirty six (35%) had triple assessment; FNAC in 106 & CB in 239. No cancers were diagnosed.

Conclusion: It would appear safe to omit FNAC / CB in patients aged under 25 years when clinical and US findings were normal or benign. This approach would have avoided triple assessment in all but 24 patients (%) in the study, avoiding the discomfort and minor complications of a needle

biopsy as well as the considerable costs associated with radiologist & pathologist time and consumables.

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Evaluation of Axillary Nodal Metastasis with High Resolution Magic Angle Proton Magnetic Resonance Spectroscopy in Breast Cancer Patients- a Pilot Study

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Background: The extent of axillary lymph node involvement in patients with cancer breast is an important prognostic marker. Prophylactic axillary dissection is associated with significant morbidity in clinically negative axilla. The intra-operative sentinel node biopsy (SNB) provides a basis for omitting the routine axillary dissection however, it has limited sensitivity and requires complicated training and infrastructure. We report the use of high resolution magic angle proton magnetic resonance spectroscopy (HRMAS) in assessing the axillary nodal status with increased sensitivity.

Methods: Axillary lymph nodes (n=17) obtained after sentinel node biopsy from seventeen individual patients were blindly subjected to 400–MHz high resolution magic angle proton magnetic resonance spectroscopy. The tissue specimens used for HRMAS analysis were sent for histopathological examination and the metabolic profile of these nodes were correlated with the routine histo-pathological findings.

Results: On histopathological examination, 7 nodes were positive for malignant cells where as no evidence of metastasis was seen in 10 nodes. The spectra of nodes (n=7) found positive for malignant cells were exclusively dominated by signals from choline, choline containing compounds at the region of 3.2 ppm and by lactate at 4.12 ppm in all the samples.

Conclusion: Metastatic and non involved lymphnodes in breast cancer can be accurately distinguished based on its chemical profile. The technique of high resolution magic angle proton magnetic resonance spectroscopy can be utilized in enhancing the sensitivity of sentinel node biopsy and may replace frozen section histopathology.

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Mammography,ultrasound and Magnetic Resonance Features of Triple Negative Breast Cancer

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Background: Triple-negative cancer is defined as: estrogen receptor negative, progesterone receptor negative and human epidermal growth factor receptor 2 negative. It is characterized as a cancer with a high malignancy potential and a poor prognosis, although on some diagnostic procedures they might have features of benign tumors. We evaluated the specific features in patients with triple-negative breast cancer using several diagnostic procedures: mammography, ultrasound (US) and magnetic resonance (MRI).

Methods: Thirty-two pathologically proven (biopsies) of triple-negative breast cancer patients were analyzed. Mammography findings of 27 patients, 17 US and 7 MR findings were retrospectively reviewed by using the Breast Imaging Reporting and Data System (BI RADS). We also included diffusion MRI into characterization of benign/malignant tumors to further characters their nature.

Results: On mammography, triple-negative breast cancer frequently are presented with a mass (85%), that has an oval or lobulated shape (86%) and circumscribed borders (48%). Spiculated margins were rare (13%). Cancers on US are more likely to present as a mass (88%) with indistinct borders (60%) and attenuating posterior echoes (33%). This cancers on MRI are presented as a mass with centripetal enhancement and wash out curve type (57%) and restriction of diffusion with apparent diffusion coefficient (ADC) less than $1.2 \times 10^{-3} \text{ mm}^2/\text{s}$.

Conclusion: Malignant nature of this tumors better correlate with ultrasound and MRI findings, than mammography alone.