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Rapid evaporative ionisation mass spectrometry towards real time intraoperative oncological margin status determination in breast conserving surgery

St John ER, Al-Khudairi R, Balog J, Rossi M, Gildea L, Speller A, Ramakrishnan R, Shousha S, Takats Z, Leff DR, Darzi A.
Imperial College, London, United Kingdom; Imperial College Healthcare NHS Trust, London, United Kingdom

Introduction:

Positive tumour margins following attempted breast conserving surgery (BCS) is an important risk factor for local recurrence. Nationally in the United Kingdom on average approximately 25% of patients undergoing BCS require additional surgery for positive margins. Traditional techniques such as specimen xray, frozen section & imprint cytology to optimise margin clearance have significant limitations. Various research methods under investigation include optical spectroscopy, high resolution imaging and radiofrequency spectroscopy. Rapid Evaporative Ionisation Mass Spectrometry (REIMS) is a new method that uses mass spectrometric analysis of the tissue specific ionic content of the surgical diathermy smoke plume for the rapid identification of dissected breast tissues as an intelligent knife (iKnife). We investigate the ability of the "iKnife" to analyze heterogeneous breast tissue intraoperatively using mass spectrometric techniques.

Method:

The study involved three stages that comprised: method development, tissue specific ex-vivo database construction and intraoperative analysis. Smoke aerosol produced as a result of electrosurgical diathermy from a variety of frozen, fresh and in-vivo breast samples were aspirated into a mass spectrometer via a modified surgical handpiece. Tissue diagnosis was confirmed by subsequent histopathological validation. The data underwent computational analysis using multivariate statistics –predominantly Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA), along with leave one patient out cross-validation. A total of 128 patients (n=40 method development, n=66 ex-vivo database, n=22 intraoperative analysis) undergoing breast surgery were enrolled in this study. Ethical approval was obtained from the Research Ethics Committee.

Results:

40 patients contributed breast samples (normal and cancerous) for method optimisation to enable analysis of high intensity spectra from heterogeneous breast tissue. Following optimisation an ex-vivo database was constructed from 89 excised fresh breast tissue samples from 66 patients using 330 spectra (246 Normal, 60 Tumour – IDC, ILC, IMC and 24 Benign - fibroadenoma). Multivariate statistical analysis of data revealed classification of tumour compared to normal tissue with sensitivities of 93.0% and specificity of 91.9%. The iKnife was used

intraoperatively during the entire operation of 25 surgeries. Spectral data was obtained within 1-2 seconds. Specific margin analysis correctly identified negative margins in 10 cases.

Conclusions:

The iKnife has been successfully developed for analysis of intraoperative heterogeneous breast tissue. Preliminary data suggests that this technique is suitable with high accuracy for the separation of normal, benign (fibroadenoma) and cancerous (invasive ductal and invasive lobular carcinoma) breast tissues. In comparison to the normal breast, cancerous tissues exhibit statistically different spectral profiles. Further work is aimed at the development of a real time algorithm able to match intraoperative data with the pre-existing database for the rapid interpretation and real time feedback of intraoperative data towards detecting positive margins intraoperatively.