Accuracy rate of Fast Raman device in determining completeness of excision of basal cell carcinoma in comparison to conventional histological assessment modalities

Aim

To determine the rate of concordance in assessing completeness of excision of basal cell carcinoma between the Fast Raman device and routine morphological evaluation using Haematoxylin and Eosin (H&E) stained frozen sections.
Histological evaluation is performed blindly by three assessors. The first assessment constitutes the "Practical Reference" (PR), where completeness of excision is determined intraoperatively by histologically-trained Mohs surgeon as in routine practice. The second assessment is performed post-operatively by two Dermatopathologist and constitutes the "Standard Reference" (SR).
Both references will be compared separately to Fast Raman results separately to determine the rate of accuracy, sensitivity and specificity.

Protocol

"Practical Reference"- Intra-operative assessment
The Mohs surgeon examines the frozen H&E sections as per standard Mohs operating procedure. Tumour is detected across multiple consecutive sections, with an average of 100 μm apart. Deeper H&E sections are examined for tumour detection until the surgeon is satisfied that a full face section of the tissue is examined and the three main skin layers are visible. Based on the interpretation of H&E sections and various external factors (quality of frozen sections, lesion location, patient age, etc.), the surgeon determines whether the basal cell carcinoma is completely excised or a further resection is needed. If tumour is detected, the surgeon marks the site of tumour on the Fast Raman map (FRM) (an illustration with the exact shape of the tissue section used by Raman device) and the serial number of the positive section is recorded. Any uncertainties that prompt a further resection, unrelated to BCC (such as inflammation, missing epidermis, etc.) are noted by the Mohs surgeon. If no BCC detected the tissue is deemed as negative (i.e. clear margins).

"Standard Reference" Post-operative assessment
The same set of frozen slides used by the Mohs surgeon will be examined post-operatively by two Dermatopathologists, independently. Consensus histopathology produced by the two Dermatopathologists will be regarded as the SR for the study. In cases where the two Dermatopathologists disagree, an external Dermatopathologist will provide an additional assessment, and will participate to a discussion to decide the most reliable SR.
As with the PR assessment, tissue sections are examined in the order of dissection (from the outer resection surface inward). Serial sections are examined until a proper full face section is obtained such that the epidermal edge, deep and lateral inked margins are visible in a single flat plane (i.e adequate section) unless a definite tumour deposit is detected on earlier section.

SR assessment will be done using a conventional microscope (similar to PR) and digitally, using a whole slide imaging (WSI) platform. For WSI, H&E slides will be scanned into high-resolution (x40) magnification using a NanoZoomer Digital slide scanner (nanosoomer.hamamatsu.com). NDP.view2 software will be used for slide viewing,

annotation and calculation of tumour surface area. Positive cases will be marked on the corresponding FRM.

The two Dermatopathologist will assess each H&E section within 4 weeks of each other, to ensure that each assessor's results are independent. At the end of the study, all slides that produced discording diagnoses will be assessed by the external Dermatopathologist all at once. A meeting will be scheduled where all three Dermatopathologist will discuss these cases to reach a consensus. The histopathological assessment schedule can be found in the corresponding document (Histopathological assessment schedule.xlsx).

The detection rate of both PR and SR will be compared with the fast Raman detection rate to measure accuracy, sensitivity and speciality.