Challenges and Frontiers in Vibrational Spectroscopy of Brain Tissue

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Cells and tissues of the brain were among the first of many different classes of tissue characterized by vibrational spectroscopy. The identification of pathological processes based on the complex chemical composition is one of the main reasons for vibrational spectroscopic studies on brain tissue. Within this context, the contribution will illustrate the impact and promise of the technique and review new applications in neuroscience.

A) Primary brain tumors

The most applications are focused on the identification and classification of primary brain tumors. In contrast to the other types of tumors, brain tissue can not be removed with a large safety distance from the tumor. A resection of brain tumors is strong limited to the border of the tumor. Therefore, clinical diagnosis of the brain tumor is at the forefront in the management of malignant tissue. This process involves surgical resection followed by the histopathological assessment of the tissue. The histological assessment must be performed quickly while surgery is ongoing in order to determine whether the tumor has been removed. A rapid and objective classification of brain tumors while surgery is ongoing is required. This can be performed by vibrational spectroscopic imaging. At several examples is demonstrated the potential of vibrational spectroscopic imaging to classify brain tumors and to distinguish tumor tissue from healthy tissue. Sophisticate approaches have been developed within the past 10 years. Consequently, spectroscopic measurements are preformed now in the neurosurgery suite. This opens also a chance for an in-situ detection of eloquent areas during the resection of the tumor.

The high success classification rate of different brain tumors by vibrational spectroscopy demonstrates the potential of the method for an objective distinction of normal from tumor tissue and, more importantly, for the grading of tumor malignancy from astrocytomas of grades II and III to glioblastomas of grade IV. Several studies encourage the pursuit of additional research to further refine this approach as an adjunct to established histopathological techniques. The technology required for these measurements is evolving rapidly, so that it is reasonable to expect that spectroscopic-based methods could be adopted into routine practice. Novel approaches using focal plane array detectors promise to yield equally informative spectroscopic maps within minutes. It should also be emphasized that once the classifier has been fully developed and validated, it is only a matter of seconds to derive spectroscopic-based histological classifications from the spectroscopic image for sample.

In conclusion, the combination of infrared spectroscopy with multivariate data evaluation and classifications methods has clear potential in providing the neurosurgery with a new rapid tool for detection and grading of brain tumors. This technique might be useful in the operating theatre as a means to identify tumor margins.

Discussion (in addition to the break out discussion topics):

Potential of FTIR microspectroscopy and/or FTIR imaging as in-vitro method in the operating room.

B) Metastasis

While this general approach has been illustrated here for the classification and grading of primary brain tumors, it is reasonable to expect that the same method will be useful in other related applications, for example distinguishing metastatic from primary tumors and possibly identifying the origin for metastases (C. Kraffts group),.

The chemical fingerprint of a metastasis is a very good indicator for the organ of the primary tumor. Indeed, several published works demonstrate that infrared spectroscopy is a successful tool to identify and classify metastases according to their origin.

C) Challenges and frontiers for in-vivo measurements

For localization of brain tumors, x-ray and nuclear magnetic resonance based imaging techniques are applied as standard. However, these techniques are not used during neuro surgery. Instead, neuro navigation, that means synchronization of the images with the patient, can assist the surgeon in intrasurgical situations. This method fails to optimize the accuracy of tumor resection because of the intraoperative brain shift. The preoperatively determined tumor margins usually do not correspond to the real time situation. Interoperative monitoring of brain tissue could improve the determination of tumor margins. For this purpose, a Raman spectrometer coupled to a fiber optic probe can be used. Recently, such a prototype Raman probe was developed for in vivo detection of dysplastic tissue in rats (G. Puppels group). However, this probe is not commercially available.

Discussion: How realistic are in-vivo measurements on the brain, even under consideration of the entire operating theatre?

D) Identification of eloquent areas

Often a function-preserving resection of the tumor is very difficult since the malignant tissue is located in the vicinity of eloquent areas. According to contemporary standards regarding tumors located in/or near eloquent areas, either the surgical removal is rejected, owing to the possible diminution of the postoperative quality of life (aphasia), or the tumor is only partially resected observing a safe border far from the eloquent brain area. The most important question of the tumor extirpation is not which tissue has to be removed but which tissue must not removed. Right now, such eloquent areas are “identified” by electrophysiological measurements or – a new approach – by optical imaging of intrinsic signals. Both methods indicate eloquent areas with an unsatisfactory sensitivity and specificity.

Discussion: Can Raman spectroscopy help eloquent areas to identify with a significant higher sensitivity and specificity as methods used?

E) Detection of other brain diseases

The determination of water concentration in brain tissue is also of high interest since brain edema is a morbidity factor. Raman spectroscopy could be an excellent tool to measure the concentration of water in brain directly. However, to my knowledge, no investigations are known.

Another large field of vibrational spectroscopy is devoted to the identification of Alzheimer’s and prion diseases (D. Naumanns group). Since vibrational spectroscopy provides fingerprint-like information with a high sensitivity small molecular differences can be detected and used for differentiation in the nuclei of nerve cells. It seems that vibrational spectroscopy can be useful to support the clinical finding of diseases with a very strong relation to clear and significant molecular changes.

Discussion: Benefit of vibrational spectroscopy in the clinical context of such brain diseases in comparison to novel methods of molecular medicine.