Ictal intracranial electroencephalography using wavelet analysis of high-frequency oscillations in Chinese patients with refractory epilepsy

HW Leung*, WS Poon, PKL Kwan, CHT Lui, TL Poon, ELY Chan, SC Yuen

KEY MESSAGES

1. Both intracranial electroencephalography and detection of wavelet-transformed high-frequency oscillations (HFOs) may be beneficial in surgery for patients with focal epilepsy.
2. Detection of wavelet-transformed HFOs may increase the percentage of patients eligible for resective surgery by 5% to 6.5%, compared with intracranial electroencephalography alone.
3. Detection of wavelet HFOs may improve surgical outcome by 17% to 18%, compared with intracranial electroencephalography alone, and by 30% if no intracranial electroencephalography is used.
4. High-frequency oscillations that are detected at the onset of seizure help determine seizure outcome.
5. Cortical areas that demonstrate hyperexcitability may be associated with HFOs.

Hong Kong Med J 2018;24(Suppl 3):S21-3
HMRF project number: 01120726

[1] HW Leung, [2] WS Poon, [3] PKL Kwan, [4] CHT Lui, [5] TL Poon, [6] ELY Chan, [7] SC Yuen

[1] *Department of Medicine and Therapeutics, The Chinese University of Hong Kong*
[2] *Department of Surgery, The Chinese University of Hong Kong*
[3] *Department of Neurology, Royal Melbourne Hospital, Melbourne, Australia*
[4] *Department of Medicine, Tseung Kwan O Hospital*
[5] *Department of Neurosurgery, Queen Elizabeth Hospital*
[6] *Department of Medicine and Geriatrics, Tuen Mun Hospital*
[7] *Department of Neurosurgery, Tuen Mun Hospital*

* Principal applicant and corresponding author: howanleung@cuhk.edu.hk

This summary is based on the study first published in: Leung H, Zhu CX, Chan DT, et al. Ictal high-frequency oscillations and hyperexcitability in refractory epilepsy. Clin Neurophysiol 2015;126:2049-57.

Introduction

Epilepsy is a neurological disease that places a heavy burden on society. Approximately 68 000 patients in Hong Kong have some form of seizure disorder,[1] and one-third of these patients have seizures that are refractory to medical treatment. Surgery may provide a cure in due course, but identification of seizure focus is necessary for success. In patients with a clear and resectable structural lesion, surgery may proceed after video electroencephalography, magnetic resonance imaging, and clinical psychological testing. Nonetheless, some patients do not appear to have a resectable lesion according to these methods.

High-frequency oscillations (HFOs) refer to electrographic activity of 80 to 500 Hz. It is hypothesised that HFOs can be biomarkers for epilepsy.[2] Wavelet transformation may accurately depict HFOs. We propose that detection of wavelet-transformed HFOs of a seizure may help determine the seizure-onset zone that is essential for epilepsy surgery.

Methods

A total of 128 patients with refractory epilepsy underwent resective surgery in our hospitals between July 2013 and June 2015. Of these patients, 15 women and 19 men (mean age, 34 years) gave informed consent to undergo intracranial electroencephalography. These patients underwent implantation of grid or strip electrodes with a range of configurations to delineate seizure foci. Episodes of stereotypic seizure with clinical manifestations were recorded in 3-minute epochs, adopting bipolar montage and good technical quality. Each epoch covered the entire seizure and centred on a quarter of its own length from the onset of seizure. Electroencephalographic findings for each seizure were first analysed visually by a neurologist, followed by off-line export of data for wavelet analysis. The number of scales that corresponded to the range of 80 to 500 Hz was used. The algorithm was generated using a MATLAB platform. The mother wavelet used was biorthogonal 6.8. The density of HFOs was calculated by a peak-to-trough power ratio of 50 to 70. If the ratio fell below 10, the electrode position might not have represented the seizure onset zone.

A previous cohort served as a pilot control group in which the percentage of patients eligible for resective surgery was 70% and the rate of good surgical outcome was 57%.[3] During the recording procedures, conventional frequency ictal patterns,

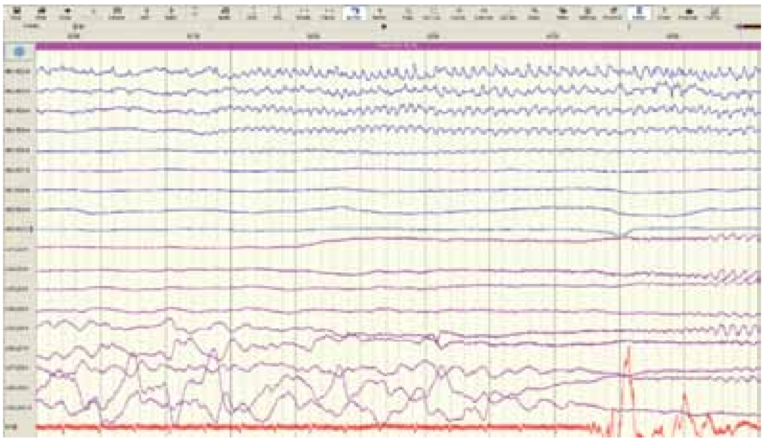

FIG 1. Electrographic record of a difficult-to-locate onset that may be amenable to testing for high-frequency oscillations

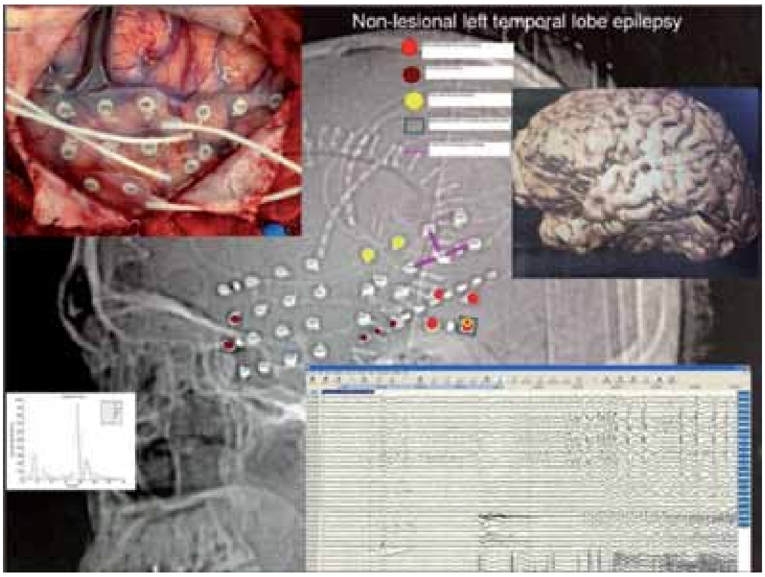

FIG 2. Sampling electrodes placed over a curvature of neocortical area and high-frequency oscillations

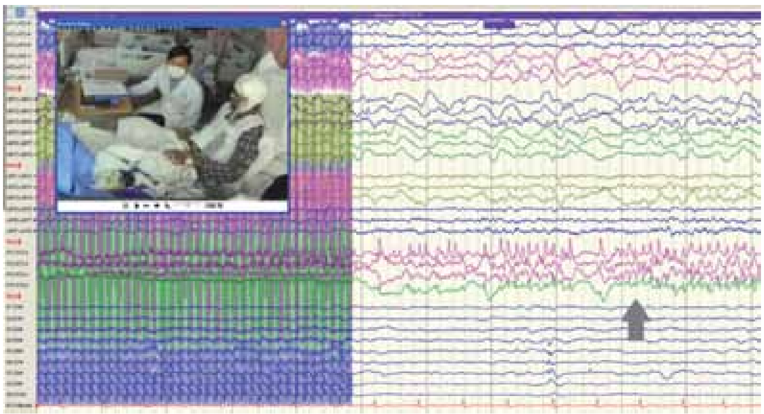

FIG 3. Conditions of hyperexcitability

hyperexcitability, and radiological lesion were also recorded.

An ancillary study included the technical aspect of electroencephalographic data. Hyperexcitability was defined as the appearance of after-discharges or clinical seizures following electrical stimulation (50 Hz, biphasic, pulse width of 0.5 ms, 5 s, 5 mA). The mean proportion of HFOs among resected channels was compared with that of the conventional frequency ictal pattern, hyperexcitability, and radiological lesion.

Results and Discussion

The proportion of patients who were eligible for resective surgery was 76.5% following review of wavelet-transformed HFOs and 75% following visual analysis of HFOs. Thus, an increase of 5% to 6.5% was expected when wavelet-transformed HFOs were analysed. The proportion of patients who attained good surgical outcome with accurate identification of seizure-onset zone was 71.4% following review of wavelet-transformed HFOs, compared with 75% following visual analysis of HFOs. This represented an increase of 17% to 18% when compared with no visual analysis of HFOs, and an increase of 30% when compared with no intracranial electroencephalography.

By testing for HFOs, we demonstrated a safe and fast methodology to determine the laterality of onset for patients with bilateral mesial temporal scleorsis (Fig 1). In patients in whom electrographic signals were sampled in the greater curvature of a neocortical surface, the number of channels involved initially may have been so extensive that rapid identification of foci was not feasible. Our mathematical representation identified the distinctive region with HFOs and added strength to information not visible to the naked eye (Fig 2). In addition, our analysis showed additional evolution of discharges throughout the seizure epoch that was not uniform. Fast activity was evident at the very first moment of the seizure, followed by a decrease in power towards the mid-portion. As the seizure epoch concluded, spectral power was regained, culminating in final, abrupt cessation of seizure. This phenomenon was not observable by visual analysis of HFOs. Hyperexcitability co-occurred with HFOs, conventional frequency ictal patterns, and radiological lesions (Fig 3).

Combining two or more modalities may improve selection of candidates for surgery. Our data suggest that when both wavelet-transformed HFOs and hyperexcitability are used, sensitivity can be maintained at 100% (95% confidence interval [CI]=0.52-1) and specificity may be increased from 66.7% (95% CI=0.31-0.91) to 75% (95% CI=0.36-0.96), compared with wavelet-transformed HFOs alone.

Our study demonstrated that by testing for wavelet-transformed HFOs, patients who would otherwise be denied surgery may receive a potential cure. Our study has used an effective research platform in electroencephalography whose results concur with those of other studies.[4,5] We are interested in ictal HFOs because they have been revealed during intracranial recordings. Identifying the moment of seizure provides researchers with the strongest evidence of localisation and lateralisation. Surgery improves seizure outcome and is feasible in refractory epilepsy, and patient quality of life can be improved. This project may improve public awareness and institutional priority and in turn, benefit patients with epilepsy.

Acknowledgements

This study was supported by the Health and Medical Research Fund, Food and Health Bureau, Hong Kong SAR Government (#01120726). We thank Ms Kwun-Lin Man and Ms Roxanna Liu for their coordination of the project, and Dr XL Zhu and Prof KS Wong for their support in all aspects of clinical research.

Ethical Approval

Informed consent was obtained from each participant.

Declaration

The authors have no conflicts of interest to disclose.

References

1. Neurology in Hong Kong 1993-2013. Hong Kong Neurological Society 2014.
2. Gloss D, Nolan SJ, Staba R. The role of high-frequency oscillations in epilepsy surgery planning. Cochrane Database Syst Rev 2014;1:CD010235.
3. Au L, Leung H, Kwan P, et al. Intracranial electroencephalogram to evaluate refractory temporal and frontal lobe epilepsy. Hong Kong Med J 2011;17:453-9.
4. Modur PN, Zhang S, Vitaz TW. Ictal high-frequency oscillations in neocortical epilepsy: implications for seizure localization and surgical resection. Epilepsia 2011;52:1792-801.
5. Ochi A, Otsubo H, Donner EJ, et al. Dynamic changes of ictal high-frequency oscillations in neocortical epilepsy: using multiple band frequency analysis. Epilepsia 2007;48:286-96.