Scientific title

Application of 3D magnetic resonance neurogram sequences for evaluation of Intraparotid facial nerves in patients with parotid neoplasm

Research protocol

Version 4

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Scientific basis

Parotid neoplasm consists of a wide range of benign and malignant lesions, and parotidectomy has been the mainstay for management of these neoplasms. Within the parotid gland there are branches of the intra-parotid facial nerves, which are tiny in calibre and are prone to injury during operation. It has been reported in recent retrospective reviews that the incidence of temporary and permanent facial nerve injury were 9.2% and 5.2% respectively, the risk of which increased with old age, malignant tumour and revision surgery [1]. Traditionally the incident of facial nerve injury is reduced by intra-operative facial nerve monitoring and surgical magnification, while imaging has limited role in aiding this purpose.

MRI is considered a cornerstone modality in the diagnosis and management of salivary gland tumours, with multi-parametric imaging providing clue to the underlying histology and relationship with adjacent structures. With the advancement of MRI, new and higher resolution three-dimensional sequences such as Dual echo Steady State (DESS) or constructive interference in steady state (CISS) sequences have been shown to better demonstrate the extracranial, intraparotid facial nerves [2-3]. More recent studies have also shown potential use of delineation of facial nerve branches in relationship to tumour [4]. However, the advantages and disadvantages of these sequences remain unknown. Our study aim to compare the efficacy between the two sequences, and also to compare with conventional 3D post-contrast anatomical imaging studies in the localization and visualization of the facial nerve branches in patients with tumour.

Reference:

1. Jin H, Kim BY, Kim H. et al. Incidence of postoperative facial weakness in parotid tumor surgery: a tumor subsite analysis of 794 parotidectomies. BMC Surg. 2019 Dec 26;19(1):199. doi: 10.1186/s12893-019-0666-6.

2. Guenette JP, Ben-Shlomo N, Jayender J. et al. MR Imaging of the Extracranial Facial Nerve with the CISS Sequence. AJNR Am J Neuroradiol. 2019 Nov;40(11):1954-1959.

3. Qin Y, Zhang J, Li P. et al. 3D double-echo steady-state with water excitation MR imaging of the intraparotid facial nerve at 1.5T: a pilot study. AJNR Am J Neuroradiol. 2011 Aug;32(7):1167-72.

4. Kim Y, Jeong HS, Kim HJ. Et al. Three-dimensional double-echo steady-state with water excitation magnetic resonance imaging to localize the intraparotid facial nerve in patients with deep-seated parotid tumors. Neuroradiology. 2021 May;63(5):731-739.

Study protocol

This study will be a prospective cohort model comparing between the efficacy of different MRI sequences in visualization of the facial nerves.

Patient recruitment

Inclusion: Consecutive patients with parotid tumour diagnosed on other imaging modalities (such as ultrasonography or computed tomography), with or without cytological diagnosis from fine needle aspiration, will be recruited from the ear, nose and throat specialty clinic.

Exclusion:

- Patients who are contraindicated to magnetic resonance imaging (such as due to underlying MRI incompatible metallic implants)
- Patient who are contraindicated to MRI contrast agents (such as advanced renal failure or previous severe allergic reaction)
- Patients who cannot cooperate for MRI scanning.
- Patients show are unable to provide informed consent.

Consent form will be signed by patient before the examination. We currently aim to recruit approximately 50 patients for the purpose of the study according to the following basis for calculation of statistical power.

> *According to previous studies, there is an estimated ~60% predication of facial nerve with conventional techniques, and ~80% visualization of facial nerves using DESS. With 80% power and two-tail alpha of 0.05, at least 42 patients will be needed according to sample size calculation.*

MRI scanning

Patient will be scheduled to be scanned at the Siemens Signa 3T MRI scanner at Gerald Choa Neuroscience Institute, the Chinese University of Hong Kong. The scanning protocol consists of conventional imaging sequences for salivary gland which includes the following sequences:

- Axial T1 weighted spin-echo
- Axial T2 weighted spin-echo (with fat saturation)
- Coronal T2 weighted spin-echo
- Diffusion-weighted imaging.
- Dynamic contrast-enhanced imaging of the salivary gland, with focus on the lesion.
- Axial post-contrat Axial T1 weighted spin-echo
- Axial post-contrast 3D T1-weighted fat-saturated SPACE

In addition, the following sequences will be performed for the purpose of facial nerve mapping:

- 3D Axial Dual-echo steady state sequence.
- Pre-contrast 3D Constructive interference in steady state
- Post-contrast 3D Constructive interference in steady state

Contrast injection will be required for these patients as per usual salivary gland MRI protocol but no additional contrast administration is required for neurogram sequences as these can be performed concomitantly. The whole scanning protocol will take approximately 45 minutes.

Image interpretation

Images will be reviewed by two independent radiologists for the conspicuity of the facial nerves. The intra-parotid facial nerve will be segmented into eight segments, which includes the main trunk (distal to stylomastoid foramen), temporofacial division, cervicofacial division, and five branches (temporal branch, zygomatic, buccal, mandibular, cervical). For each branch, its conspicuity is measured objectively by ratio between the average signal intensity of the nerve as compared to the both the parotid parenchyma and the tumour on the respective sequence. Visual assessment of the nerve is also performed using a three point scale: 2. Whole intraparotid course of the concerned segment/ branch of facial nerve identified with certainty, 1. Partial visualization of the concerned segment/ branch of facial nerve, and 0. Particular branch cannot be identified. The process will be repeated on the DESS, post-contrast CISS and conventional 3D VIBE sequences for bilateral facial nerves for each patient.

Inter-observer agreement between two observers are calculated using kappa statistics. The measured statistics of subjective and objective conspicuity are evaluated using statistics software (SPSS) using two-way comparison tests (Mann-Whitney U or two-smaples T test) as well as analysis of variance (ANOVA).

Handling and Storage of personal data

Images of usual salivary gland MRI sequences (excluding DESS and CISS sequences) will be uploaded to patient's electronic patient records for clinical use. The research sequences will be stored in the database only, except when the research sequences have impact on clinical management then selected images can be uploaded to ePR for illustration.

All MRI scans will be stored in the picture archiving and communication system of Gerald Choa Neuroscience Center/ Prince of Wales Hospital. These images can be viewed on HA clinical workstations for the purpose of providing clinical care. Radiologist with training in Head and Neck or Neuroradiology will issue a formal radiology report regrading in the examinations, the report will be available on the ePR system.

The MRI data will be anonymized and encrypted before research analysis, which will also be done in HA clinical workstations. MRI scan data after anonymization will be stored in CUHK MRI data repository, with only non-identifiable patient particulars (age, sex, disease status) retained (informed consent obtained from patient prior to scanning). Use of selected images for publication purposes will be anticipated, patient particulars will be removed prior to exporting from HA clinical workstations.

Compliance with Guidelines of Good Clinical Practice by International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use (ICH-GCP) and Declaration of Helsinki

This clinical trial is conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

This trial offers additional diagnostic benefit without known added clinical risk on top of usual clinical care. The rights, safety, and well-being of the trial subjects are the most important considerations and will be prevailed in the current study. No non-clinical use of product is involved in this study. The radiological examination subjects underwent are provided by qualified medical practitioners with adequate training in radiology.

All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.