

Supplementary protocol 1. Endoscopy protocol for HDGC

1. Annual endoscopy is recommended ideally in a centre with an interest and experience in HDGC.
2. Endoscopy to be performed using high definition zoom gastroscope and use of mucolytics such as N-acetylcysteine is encouraged to obtain good visualization.
3. Inspect and photograph the entire gastric mucosa paying particular attention to any focal lesions.
4. Clinical biopsies:
 - Take antral biopsy for rapid urease breath test (CLO-test) or for (immuno-)histochemical analysis at first surveillance endoscopy for *H. pylori* status.
 - Biopsy focal lesions for clinical histopathology and record the anatomical position of any lesion (see below).
 - Regardless of targeted biopsies taken now proceed to biopsy each gastric anatomical area in turn, taking five samples from each area:
 - a. Prepyloric area
 - b. Antrum
 - c. Transitional zone
 - d. Body
 - e. Fundus
 - f. CardiaTotal: approximately 30 biopsies
5. Research biopsies: provided that the patient has given informed consent an additional biopsy should be taken from focal lesions and each anatomical area.

Endoscopic evaluation of new modalities such as trimodal imaging or confocal microendoscopy should be done in the context of a research protocol.

Routine Clinical Biopsy processing:

1. Record position of biopsy by anatomical area and cross sectional circumference (by dividing circumference into four equal parts: lesser curve, greater curve, anterior wall, posterior wall) and give distance in cm from the teeth e.g. gastric body, greater curve at 50 cm.
2. All clinical specimens from each anatomical area should be separately labelled and sent to the histopathology laboratory with clinical information stating that this is a screening procedure to look for microscopic *foci* of signet ring cells in a patient that fulfils the IGCLC criteria for HDGC.