1.9 AIMS OF THE THESIS

The central hypothesis underlying this thesis is that hypoxia plays a role in the aetiology and prognosis of oesophagogastric cancers. The initial aim of the project was to establish databases comprising patients with surgically treated oesophagogastric cancer to examine routine clinical prognostic factors before using the database for molecular marker studies.

There is a need for accurate methods of determining prognosis in patients with these cancers; for the selection of patients for surgery, neo-adjuvant therapies, post-operative oncological therapies and non-operative intervention. The prognostic utility of tumour length and involvement of the CRM have not been fully explored as clinical prognostic markers in oesophageal cancer. It is essential that potential clinico-pathological factors are fully assessed and understood so that molecular marker studies are carried out allowing for potential confounding factors. If assessed in this way the results of prognostic studies can be more generalisable to routine clinical practice (McShane et al. 2005).

Gastric and oesophageal carcinogenesis progress through well defined sequences of events, which can be evaluated using immunohistochemistry of endoscopic biopsy specimens. HIF-1α and other associated hypoxia markers have been implicated in the aetiology of a number of cancers but have not been fully assessed in oesophagogastric tumours.

The relationship between HIF-1α and associated hypoxia markers and treatment outcome in oesophagogastric adenocarcinoma has not been evaluated so far. In addition, there are currently no published studies that have attempted to measure the oxygenation status of oesophagogastric adenocarcinoma. This is of interest because assessment of the oxygenation status in these tumours may provide prognostic information or allow the development of novel treatment approaches.

The specific aims of this thesis were to:

- Investigate the relationship of tumour length and CRM with other histopathological variables together with survival in patients with surgically treated oesophageal malignancy.

- Establish a large retrospective database of patients with gastric and gastro-oesophageal junctional cancer; analyse relevant clinico-pathological prognostic factors as a preliminary exercise prior to immunohistochemical prognostic factor analysis.

- Investigate HIF-1α and HIF-2α as prognostic markers in gastric and gastro-oesophageal junction cancer.

- Investigate HIF-1α and other related markers (HIF-2α, Epo, Epo-R, Glut-1, Ki67, VEGF) in oesophageal and gastric adenocarcinoma aetiology.

- Establish a prospective study to investigate hypoxia (by pimonidazole staining) in patients with oesophageal and gastric adenocarcinoma.