BSc in Reproductive & Developmental Sciences &

BSc in Surgery and Anaesthesia Project Outline 2011-2012

**Project Title:** Metabolic phenotyping in the surgical management of Breast cancer

**Academic Supervisor: Mr James Kinross**

**Division: Surgery**

**Section: Biosurgery and Surgical Technology**

**Co-supervisors: Dr Beatriz Jiménez, Mr. Daniel Leff**

**Who will be responsible for day-to-day supervision? James Kinross**

**Contact Details of Person whom Medical Student should contact for further details:**

**Name: Email: Tel:**

**James Kinross j.kinross@imperial.ac.uk**

**Group’s Research Interest:**

**Systems metabolism and surgical phenotyping**

(Double click the appropriate check box to indicate your choices below)

**Is this a clinical [ ]  or laboratory x project?**

**Suitable project for: Reproductive and Development**  **Sciences** Yes **[ ]** No**x**

**Surgery and Anaesthesia** Yes **x** No **[ ]**

**Synopsis of project (background/research question/methods to be used/relevant key references):**

* **Background**

Over 46,000 cases of breast cancer are diagnosed each year in the UK. The treatment is multi-modal, although surgery is a key treatment strategy. Over 56,000 mastectomy and wide local excision procedures were performed in the UK for all breast diseases in 2010. However, surgery is associated with significant co-morbidity, and 30% of cases have positive resection margins at histological analysis. The sensitivity and specificity of such techiques as sentinel lympyh node biopsy also remain variable. Systems biology approaches have yet to be adopted in breast surgery. Metabonomics describes the computational analysis of spectral data to provide information on time specific metabolic changes across a complex system. This is based on technologies such as Nuclear Magnetic Resonance (NMR) spectroscopy and Mass Spectrometry (MS) which provide a deeper understanding of diseases and are proven tools for biomarker discovery. They are also highly efficient, rapid and cost effective. By focusing multiple metabolic measuring technologies on the patient during surgery, diagnostic accuracy is increased and surgical decision making is enhanced.

* **Research Questions**

Can systems biology approaches such as metabonomics speed up tumour diagnosis and help decisions taken during surgery?

Is High Resolution- Magic Angle Spinning (HR-MAS) NMR an adequate technique to enhance diagnosis realised during surgery?

* **Methods to be used**

This study will apply a novel metabonomic strategy to the surgical management of breast malignancy.

Samples from women undergoing breast tumour resection will be obtained from tissue belonging to the tumour, margins and lymph nodes. We will also collect blood serum and urine samples from the same patients, pre- and post-operative. Tissue samples for the metabonomics study will be prepared by the histopathology team, and matching tissue samples assessed by regular approaches prior to metabonomics analysis. Clinical parameters of urine and blood serum will also be recorded after the biochemical assessment.

HR-MAS 1H NMR spectroscopy will be applied directly uponacquired tissue specimens for real time analysis 2,3 Biofluids will also be studied by HR NMR which requires minimal sample preparation.4 The resulting suite of metabolic profiles will be analysed by multivariate statistical approaches to obtain relevant biochemical and biomarker information.

By creating a deep and highly personalised metabolic overview of an individuals cancer through the use of the aforementioned approaches, this work aims to improve patient outcome after breast cancer surgery.

* **Relevant Key References**

1. Kinross JM, Holmes E, Darzi AW, Nicholson JK. “[Metabolic phenotyping for monitoring surgical patients.](http://www.ncbi.nlm.nih.gov/pubmed/21596428)” *Lancet*. **2011**, *377*, 1817-9.

2. Sitter B, Bathen TF, Singstad TE, Fjøsne HE, Lundgren S, Halgunset J, Gribbestad IS. “[Quantification of metabolites in breast cancer patients with different clinical prognosis using HR MAS MR spectroscopy.](http://www.ncbi.nlm.nih.gov/pubmed/20101607)” *NMR Biomed*. **2010**; *23*, 23424-31.

3. Beckonert O, Coen M, Keun HC, Wang Y, Ebbels TM, Holmes E, Lindon JC, Nicholson JK. “[High-resolution magic-angle-spinning NMR spectroscopy for metabolic profiling of intact tissues.](http://www.ncbi.nlm.nih.gov/pubmed/20539278)” *Nat Protoc.* **2010**;*5*, 1019-32.

4. Beckonert O, Keun HC, Ebbels TM, Bundy J, Holmes E, Lindon JC, Nicholson JK. “[Metabolic profiling, metabolomic and metabonomic procedures for NMR spectroscopy of urine, plasma, serum and tissue extracts.](http://www.ncbi.nlm.nih.gov/pubmed/18007604)” *Nat Protoc.* **2007**, *2*, 2692-703.

Prospective students do not require any previous skills in advanced multivariate computing or NMR. All samples will be collected prior to the commencement of the project.

This will be a prospective study however, with a matched control sample population.

Will the research involve work done under the Animals (Scientific Procedures) 1986 Act? Yes **[ ]** No **[x]**

**If YES*,***

Will the student be required to undergo Home Office training? Yes **[ ]** No **[x]**

Are the appropriate project and personal licences in place? Yes **[ ]** No **[ ]**

**Project licence**:

Licensee

Date of issue

Number

**Personal licence**:

Licensee

Number

**Will the research involve the use of genetically modified tissue?** Yes **[ ]** No **[x]**

**If YES**

Has the work been approved by the relevant GM Committee Yes **[ ]** No **[ ]**

Date approval was granted

Reference Number

**Will the project involve work on human subjects, human tissue or access to confidential patient information?** Yes **[x]** No **[ ]**

## If YES

## has ethical approval been obtained Yes [x]  No [ ]

## Date approval was granted 11/08/2011

## IC REC or IRAS REC number South East London 11/LO/0686

**Note: Approval for any of the above MUST be in place before the student begins the project.**

**A risk assessment form will be required.**

**Project Payment**: I have an F account Yes **[ ]** No **[ ]**

## If you have an F account please give full account code: