Background & Aims

- Glioblastoma multiforme (GBM) is a WHO grade IV malignant brain tumour with a median of 14 month survival time and a 100% mortality rate.
- Current standard-of-care therapy for GBM is surgery with concurrent chemoradiotherapy 4 weeks later; however reoccurrence is certain, usually within 2 cm of the surgical resection margin.
- Local delivery of a multitude of chemotherapeutics immediately after surgery may enhance residual disease exposure to therapeutic doses and potentially kill any remaining cells within the brain parenchyma.
- The aim of this work is to develop a novel drug delivery system which sprays etoposide (ETO) and olaparib (OLA) nanoparticles held within a bio-adhesive gel (pectin), accurately onto the surgical resection margin, ensuring brain parenchyma penetration and controlled drug release.

Polymer coated nanoparticles

- Polymer coating etoposide and olaparib nanocrystals gives high drug loading and suitable NP properties for brain delivery.

Bioadhesive gel

- In vitro biocompatibility assays show pectin is non-toxic to human astrocytes and human blood.
- In vivo studies show no adverse effects from Pectin.

TEM images show physical structure of polymer coated nanoparticles is different to drug or polymer alone.

Conclusions and Future work

- Pectin was found to be non-toxic to human derived astrocytes below 100 µM for 48 hours.
- A haemocompatibility assay showed no significant lysis of RBCs when incubated with gel for 1 hour.
- In vivo results showed no initial signs of toxicity from the 200 µM gel for 2 weeks.
- Polymer coated ETO and OLA show superior drug loading and show different physical structure to NPs alone.
- OrbiSIMS methodology is optimised to show penetration of drugs in brain tissue.
- Future work will trial safety and efficacy in vivo.
- OrbiSIMS will be employed to assess penetration of drugs using the spray device versus injected control in ex vivo and in vivo brain tissue.