

## CIRCULATING TUMOUR DNA FOR CANCER PROGNOSTICATION

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Nasopharyngeal carcinoma (NPC) is a squamous cancer of the head and neck which affects the nasopharyngeal epithelium. Since NPC cells express Epstein-Barr Viral (EBV) genes, a double-stranded DNA herpes virus, its tumours release circulating tumour DNA (ctDNA) containing EBV into circulation. Despite having uses for detection, staging, and screening, plasma EBV DNA analysis is particularly useful for post-treatment prognostication, or assessment of disease course. Due to the positive relationship between plasma EBV DNA concentration and tumour volume, EBV DNA clearance after radiotherapy is predictive of treatment outcome. Detecting small amounts of DNA is vital. The purpose of this project is to assess the current practice of using quantitative polymerase chain reaction (qPCR) or droplet

digital PCR (ddPCR) to interrogate a specific gene associated with EBV, as this has a false positive rate of 7%. ddPCR, which measures absolute nucleic acid quantity by counting molecules encapsulated in discrete, volumetrically defined partitions, is hypothesized to have a similar detection limit as qPCR. First, genomic DNA (gDNA) from an EBV+ cell line and EBV- cell line are isolated, purified, and sheared. Then, variable amounts of EBV DNA are detected using either qPCR or ddPCR. The results show that the size-selected EBV+ and EBV- gDNA are approximately 200 base pairs, and that qPCR and ddPCR have similar detection limits for the EBV genome. In conclusion, more sensitive DNA quantification techniques than qPCR and ddPCR are needed for clinical use.

## TIME DURATION OF INTRAOPERATIVE TOURNIQUET APPLICATION IS A RISK FACTOR FOR POSTOPERATIVE VENOUS THROMBOEMBOLISM IN KNEE REPLACEMENT PATIENTS

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Background: A common complication following total knee arthroplasty (TKA) is the formation of blood clots (venous thromboembolism or VTE). Clotting begins in the leg and can travel to the lungs, leading to respiratory distress and even death. Rivaroxaban is a common blood thinner used to prevent postoperative VTE. Despite this practice, some patients still develop VTE, with clinical features seemingly preceding rivaroxaban administration. As rivaroxaban can only prevent new clots from forming after administration, clot formation may be attributed to factors during the surgery, before the drug is given.

Objective: The aim of this study was to evaluate the intraoperative factors that were associated with VTE following TKA despite rivaroxaban administration.

Methods: We conducted a retrospective case-control study in Hamilton (2013-2015). Patients who received rivaroxaban but developed VTE

within 14 days of TKA were identified. Each index patient was matched to two controls who were receiving rivaroxaban but had no VTE complication. Patients' demographics and medical histories and the duration of tourniquet application were extracted.

Results: Seven postoperative VTEs were identified from a total of 234 patients. During the surgery, the index cases had a significantly longer tourniquet application time than the controls ( $65 \pm 3.3$  min and  $49 \pm 2.4$  min, respectively). There were no intraoperative complications and no noticeable differences in blood loss.

Conclusion: This study illustrates that intraoperative factors such as prolonged tourniquet application are associated with postoperative VTE, explaining the failure of rivaroxaban. We suggest a reduction in tourniquet application time as well as more emphasis on pre-surgical anticoagulation treatment.

## EFFECT OF NANO-STRUCTURED GLASSY FILM TOPOGRAPHY ON MACROPHAGE FUNCTION

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The host immune response against foreign materials, also known as the foreign body response, poses a significant challenge for implanted biomaterials and medical devices. Macrophages and dendritic cells play a crucial role in the immune response. Thus current efforts are being made to modulate their activity and behaviour in vivo. We hypothesize that surface topography in the biological scale (nanometer to micrometer range) can modulate macrophage function, specifically phagocytosis, without necessitating the use of bioactive agents. In our study, we investigate the effect of topography using a novel, nanostructured glassy film, synthesized through the deposition of 2-50 nm of silicon dioxide on pre-stressed polystyrene. The glassy film is further subjected to high heat,

inducing substrate shrinkage. The compressive stress of the shrinking substrate induces the formation of complex structures on the material surface. Murine bone marrow-derived macrophages were subsequently seeded onto the surfaces and incubated with *Streptococcus pneumoniae* bacteria to evaluate the effect of topography on macrophage phagocytosis. Fluorescent images showed increased phagocytic ability of macrophages cultured on the structured surfaces in comparison to flat surfaces. Both the extent and homogeneity of bacterial uptake improved in macrophages cultured on the glassy films. It was concluded that surface topography can passively modulate macrophage behaviour in vitro and serves as a promising avenue of study for the future development of novel biomaterials.