Monitoring vascular markers of joint inflammation in a rabbit model of rheumatoid arthritis

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Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disease afflicting 1% of Canadians. If not quickly and adequately treated, the disease can lead to functional deterioration and profound disability. There is no cure for RA; however, the advent of biological drugs – which can slow and even halt the progression of joint damage – have revolutionized its treatments. Due to the limitations of current treatment monitoring methods, drugs are administered for prolonged periods of time before their efficacy can be reliably assessed. Following this time, 30% treatments are still found ineffective, new medications are prescribed, and the process is repeated.¹ This imposes a loss of time and money on both the patient and healthcare system. There is clearly a need for a monitoring technique that can reliably assess early treatment response.

Principal Objectives: Optical technologies provide cost-effective methods of measuring vascular response; they operate non-invasively and use non-ionizing radiation. We have developed a near-infrared spectroscopy (NIRS) system that can accurately measure hemodynamics and hematocrit content. Our objective was to test its sensitivity in an animal model of RA, proving that characterization of vascular changes can aid in monitoring treatment efficacy within RA patients.

Methods: Experiments were conducted on 4 adult male New Zealand white rabbits, using an animal model of inflammatory mono-arthritis. Joint inflammation was induced in the right knees of the rabbits by repeated intra-articular injection of 0.1 mL of a 2% of λ-carrageenan solution over a 4-week period. This model has shown to produce an inflammatory response similar to human RA. The left knees were injected with 0.1 mL of saline as a control. All procedures were carried out while the animals were anesthetized with 3% isoflurane. NIRS measurements were acquired using lasers, emitting in the near-infrared, interrogating the knee joint. Utilizing the absorption properties of hemoglobin, concentrations of oxy and deoxy hemoglobin (HbO₂, Hb) and oxygen saturation (StO₂) were computed from the NIRS measurements. Joint blood flow (BF) was also measured using dynamic contrast-enhanced (DCE) NIRS – similar to DCE-MRI and CT.

Results: Hb, HbO₂, StO₂, and BF measurements were grouped into baseline (before injection), acute (<1 week following injection), and chronic (>1week) periods. Statistically significant changes (p-value <0.05) in Hb, StO₂, and BF were observed between inflamed and control joints at chronic phases as well as acute for BF. Hb, StO₂, and BF showed a percent difference of 34%, 16%, and 71%, respectively.

Discussion and Conclusions: The RA joint is known to be a hypoxic environment, which is in agreement with our findings of decreased StO₂. As well, the higher BF in inflamed joints is a direct consequence of their known higher metabolic demands. The results of this study demonstrate that NIRS can quantify vascular and hemodynamic response to inflammation. The sensitivity of these physiological parameters to joint inflammation suggest that this technology could monitor treatment efficacy in RA and most importantly, provide early assessment of treatment response. Such a method will save time, money and ultimately lead to improved clinical outcomes.