EASING PATIENT EXPERIENCE

This Trainee’s research is working towards better treatment of one of the most malignant and incurable of cancers.

WITH KAREN MURPHY

Neurosurgery Trainee Dr Iwan Bennett has spent the past three years conducting research to identify vascular biomarkers in glioblastoma multiforme (GBM), one of the most malignant and incurable of cancers, which causes half of all patients to die within little more than a year of diagnosis.

Known to be one of the most vascular cancers found in humans, Dr Bennett has been working to design minimally-invasive vascularity testing protocols which could allow clinicians to understand which patients would be most likely to benefit from the use of novel anti-angiogenic therapies.

First developed in the mid-2000s, anti-angiogenic drug therapies target the blood supply to tumours and are now either approved for use or under investigation for a range of malignancies in Australia and around the world.

Yet, while anti-angiogenic therapies such as Bevacizumab (Avastin) have been approved for use in the US for the treatment of recurrent GBM, such agents have yet to receive approval for use in GBM in Australia.

Dr Bennett said that vascular proliferation was one of the hallmarks of GBM due to an up regulation of proteins involved in the development of angiogenesis, prototypical of which were vascular endothelial growth factor (VEGF) and its receptor VEGFR-2.

He said that until now, the gold standard for assessing GBM vascularization had been to look at the amount of blood vessels in tissue under the microscope which could only be done via a craniotomy.

He said, however, that he had set out to research other means of studying vascularity such as via less invasive blood tests as a way to help ease the treatment experience of already overburdened patients.

Using blood and serum samples taken from patients with high grade glioma and healthy volunteers as controls, Dr Bennett investigated a range of biomarkers including circulating endothelial cells (shed from proliferating tumour vasculature), circulating endothelial progenitors (mobilised from bone marrow) and serum VEGF.

He also conducted Perfusion MRI tests, an advanced MRI technique which can assess haemodynamic properties within the parenchyma of the brain.

“Despite appearing identical under light microscopy, GBMs are a heterogeneous group of tumours with varying degrees of aggressiveness and responsiveness to treatment,” Dr Bennett said.

“We believe that biomarkers of GBM vascularity may provide an objective means of sub-classifying GBM and be of use in both the selection of patients most likely to respond to novel anti-angiogenic agents as well as allowing clinicians to monitor response to treatment in real time.

“So far we have demonstrated that circulating endothelial cells (CECs) are significantly elevated in patients with GBM as compared to controls and that these levels decrease post-operatively as would be expected.

“However, while CECs do not appear to be predictive or prognostic in patients receiving conventional therapy such as surgery, chemotherapy and radiation therapy, their true utility could be for patients receiving anti-angiogenic therapy.”

A novel parameter

As part of his PhD research being conducted through the University of Melbourne’s Department of Surgery and the Royal Melbourne Hospital, Dr Bennett also helped develop a novel parameter to measure the amount of vascularization within a given tumour.

He said the new measurement method had been dubbed the “cerebral blood volume (CBV) load” by the research team.

“Our parameter uses advanced MR imaging to determine the total amount of vascularization within a given tumour but its significance will depend on the ease of calculation so that clinicians can use it on a day-to-day basis and its usefulness in patient care,” Dr Bennett said.

“Unlike many novel parameters of tumour perfusion being developed by other research groups, CBV load is an easy parameter to calculate.

“Any researcher or clinician already analysing perfusion MRI for quantitative data could calculate our parameter in just a few steps with software and techniques they are already likely to have.

“However, the key to the usefulness of this parameter will depend heavily on the development of anti-angiogenic therapy for the treatment of GBM.

“Nevertheless, it provides an ideal method of non-invasively monitoring the tumour vasculature and could be of use in both patient selection and monitoring of treatment.

“We have shown that the degree of reducton in CBV load following anti-angiogenic therapy persists survival in a study of 15 patients, but this will need to be confirmed in larger studies.”

Dr Bennett’s research has been supported by the College through funding attached to a Foundation for Surgery Scholarship which he received for 2013.

His PhD thesis is being supervised by neurosurgeon Dr Andrew Morecroft, from the University of Melbourne and the Royal Melbourne Hospital as well as Associate Professor Christopher Hovens, a published researcher in the field of vascular biomarkers in prostate cancer.

He said he felt particularly fortunate to have been able to conduct his research through the University of Melbourne’s Department of Surgery located as it was in the Clinical Science Building of the Royal Melbourne Hospital campus.