Childhood Eye Cancer Trust
Fighting Retinoblastoma

Final Report

Research projects funded by the Childhood Eye Cancer Trust

All information provided in this report will be kept confidential to the Childhood Eye Cancer Trust, unless stated

Name: Dr. Clare Wilson

Date: 1st November 2017

Project title: *Retinal vessel architecture in retinoblastoma patients - a predictor of progression*

Date awarded & value: Jan 2013 £10,500

Amount claimed to date: £4,500

We hereby declare that we shall not be invoicing for any more funds from the CHECT and would be very pleased for the remaining funds to be released to sponsor other important research into retinoblastoma, as per the experienced discretion of the CHECT scientific advisory board.

Aims / Objectives of project:

To study the feasibility of using semi-automated digital image analysis of vessel parameters including retinal vessel tortuosity and width to aid detection of tumour progression.

Summary of Project for CHECT Scientific Advisory Committee:

The project milestones were divided into three parts with a “Supplementary Section” (1) agreed after awarded grant, as we were keen to go from semi-automated to totally automated vessel parameter analysis. A further supplementary section (2) was subsequently also added to automatically measure tumour size as a necessary parallel to vessel changes with disease progression/regression.
For ease in this document I have translated the above in to 5 milestones to report.

Milestone 1

Compilation of spreadsheet detailing all patients to be included in study with respective images associated from the RetCam Bank, coupled with the demographic details and

Milestone 2

Each image was analysed using CAIAR (Computer Aided Image Analyis of the Retina), semi-automated retinal vessel analysis software. A trainee ophthalmologist (KW) pixelated each significant retinal vessel supplying the tumours on each of the retinal images. The software then determined the vessel width and tortuosities from each vessel.

Milestone 3

The data collected in milestone 2 was analysed to assess whether there was any difference in widths and toruosities in retinal vessels before and after retinoblastoma treatment.

The studies from milestones 1,2 and 3 resulted in presentation of a poster at ARVO in May 2014 (Figure 1).

Presentation Number - Posterboard Number: 3083 - A0016
Abstract/Presentation Title: Retinal vessel architecture in retinoblastoma pre and post treatment
Session Number: 336
Session Title: Non-melanoma intraocular lesions: Retinoblastoma and beyond
Session Date/Start Time: May 6, 2014 from 11:00 AM to 12:45 PM

CONTROL ID: 1913761

TITLE: Retinal vessel architecture in retinoblastoma pre and post treatment

AUTHORS (LAST NAME, FIRST NAME): Wilson, Clare[1, 2]; Wong, Karen[3]; Sagoo, M. S.[3]; Reddy, M Ashwin[3]

INSTITUTIONS (ALL): 1. Ophthalmology Department, Great Ormond Street Hospital, London, United Kingdom.
2. Department of Vision Science , UCL Institute of Ophthalmology, London, United Kingdom.
3. Ophthalmology, Barts Health, London, United Kingdom.

ABSTRACT BODY:
Purpose: This study aimed to quantify the vessel parameters including width and tortuosity in patients with retinoblastoma before and after treatment.
Methods: 20 RetCam images from 10 children diagnosed with retinoblastoma at Royal London Hospital were analysed. The sentinel vessel width and tortuosity values were analyzed with semi-automated software CAIAR (Computer Aided Image Analysis of Retina) at the time of diagnosis and after effective treatment. Data were analyzed with two tailed paired-t test.
Results: The mean width of sentinel vessel pre-treatment is 2.59 and post-treatment is 1.60 (p= 0.001; SD= 1.07); the mean tortuosity value of sentinel vessel pre-treatment is 2.55 and post treatment is 1.19 (p=0.011; SD= 2.02). The sentinel vessel width and tortuosity value were significantly less after effective treatment.
Conclusions: Prompt treatment is paramount to saving the eye and preventing death from metastasis in retinoblastoma. Retinal vessel width and tortuousity decreases with disease regression. Following further study, the quantification of retinal vessel architecture may be of use as a valuable screening tool, predictor of disease progression and assessment of treatment response in retinoblastoma patients.

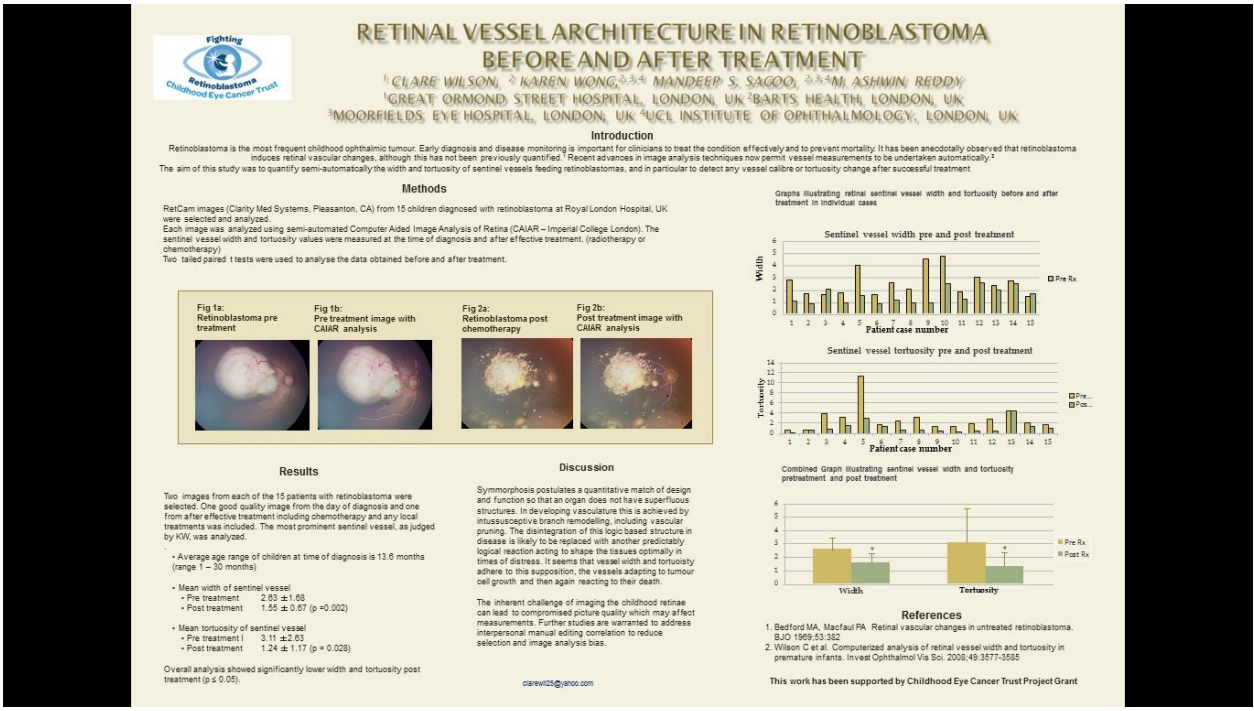

Figure 1 ARVO Presentation May 2014

Milestone 4

Detection of vessel changes using automated analysis software

As human vessel pixelation is not a viable bedside option as it is timely and costly requiring expert input, we developed software that can automatically detect the vessels in retinal images from eyes with retinoblastoma. Previous work in our team has developed software to analyse retinal images in babies with retinopathy of prematurity. One of our challenges with the retinoblastoma images was in finding the optic nerve. This is the first step for analysis of preterm retinal images, and is complicated in retinoblastoma images by the relative similarity to image analysis algorithms of an optic nerve head and a retinoblastoma tumour. The solution to this issue and resulting traces of vessels exemplified in figure 2.

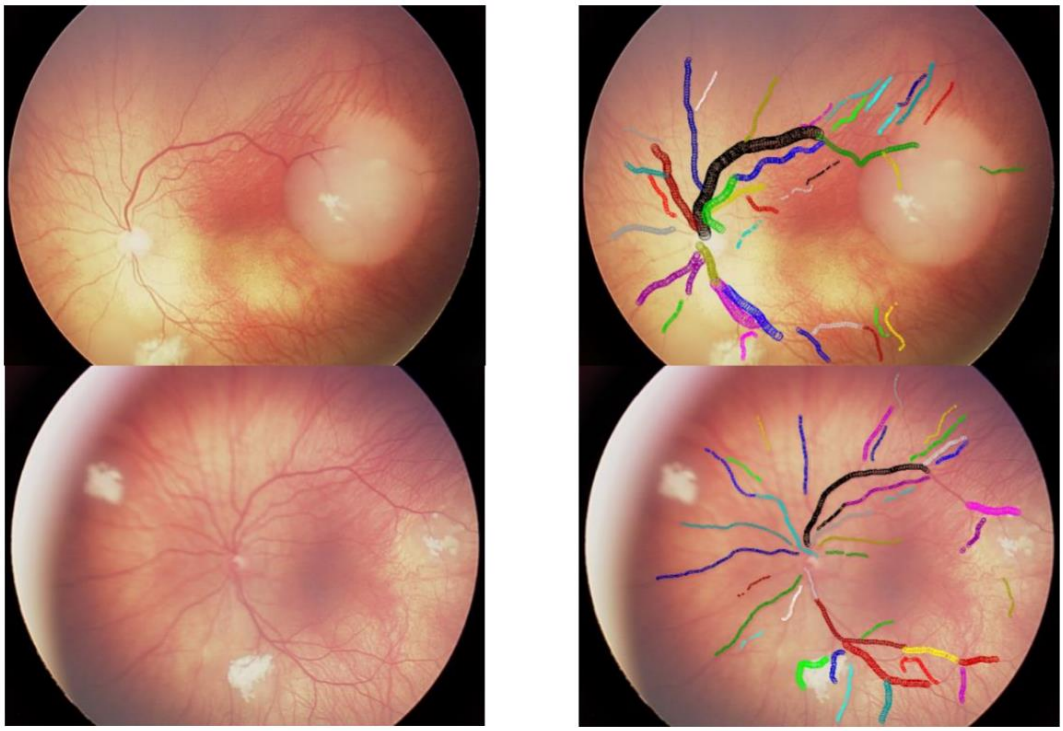

Figure 2 An example automated vessel segmentation. The vessels feeding the lesion tend to become tortuous (twisted), for example the blue artery in the pre-treatment image (top right). The same vessel can be seen to have straightened in the post-treatment image (bottom right – now purple). In addition the vessels have reduced in width after successful treatment.

We analysed a set of 9 pre- and post-treatment images. From the images we calculated the width, tortuosity and angle of vessels. Width and tortuosity are seen to clearly reduce in some cases (see the above image). This is encouraging and suggests these measures may identify patients in need of further treatment.

Milestone 5

To accurately quantify the prediction of vessel architectures in relation to tumour progression, an automated technique to quantify tumour size was required.

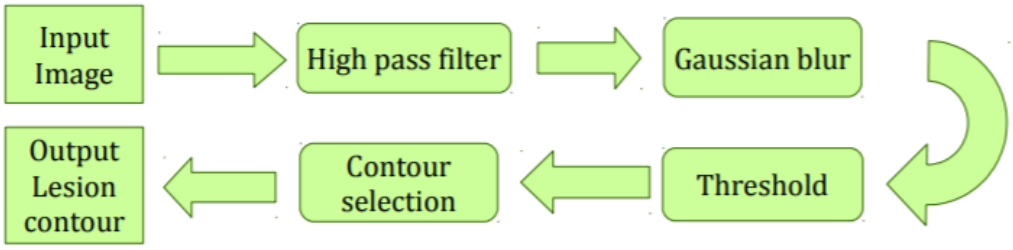

Figure 3 Image processing steps to achieve tumour localisation

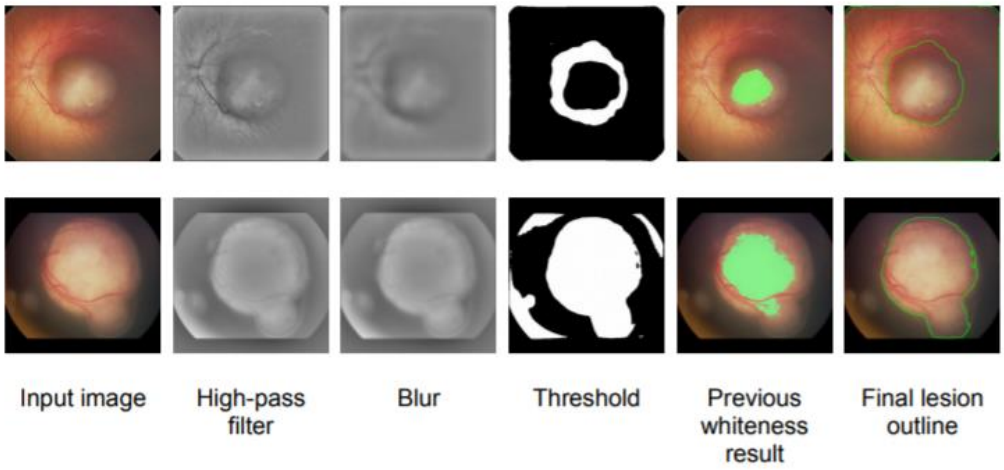

Figure 4 Two images from eyes with retinoblastoma showing successful automated lesion outlining

Future Research

We are extremely grateful to the financial contribution from CHECT to perform this work. This grant has enabled us to demonstrate a scientific basis for the proposed relationship between retinal vessels and retinoblastoma characteristics. It has also enabled us to develop techniques for automated detection of retinal vessels and tumours in images from children with retinoblastoma which may be clinically useful in the future as an instant cotside test. We hope to plan future research into the more detailed relationship between the vessel changes and tumour advancement/regression to provide automated software to aid detection and monitoring of retinoblastoma. Unfortunately within our current small team we do not have the time to progress this further due to other demands, and are therefore drawing this grant to a close, with a strong hope of returning to this work when we have the resources to do it justice.

Lay summary for CHECT general committee:

Retinoblastoma treatment has developed leading to vastly improved survival rates. However, detecting early disease progression is challenging for experienced retinoblastoma surgeons who see over 20 new patients a year. It is even more problematic for surgeons working in countries with smaller populations. An objective assessment that can alert the surgeon to progression of the cancer would be of great benefit.

New software can measure changes in blood vessels at the back of the eye. Eye cancer doctors have made the clinical observation that these vessels change when disease worsens, and so could be used to detect eye needing more treatment. At The Royal London Hospital we have a large set of digital images from children who have had eye cancer and we are analyzing them with new software to see if the vessel changes can be used to accurately detect progression of the tumour.

We have found that the retinal vessels do change with disease progression and could be used to detect eyes that may go on to suffer recurrence to disease after treatment. In this study we have developed software specific for automated retinal vessel detection and quantification aswell as software to automatically detect and evaluate tumour size. Future work could involve a prospective study looking at the vessel changes in children undergoing retinoblastoma treatment, taking their images for analysis of the vessels and tumour size in parallel.