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**AUTOMATED MEASUREMENT OF THE DENSITY OF VESSELS ON WHOLE SLIDE IMAGES OF PAEDIATRIC BRAIN TUMOURS**

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**Introduction/ Background**

Microvasculature is known to have a prognostic significance in many brain tumours. It is important to be able to quantify it in a reproducible way on biopsy samples and, if possible, through noninvasive imaging techniques.

**Aims**

A quantitative and reproducible way to assess the microvasculature of biopsy samples of human paediatric brain tumours is needed, in order to help diagnosis (possibly give a hint of the grading of the tumours) and to see if a correlation exists with a perfusion MRI (ASL) signal. The method should be applicable to standard whole-slide images of samples immunostained with CD34 marker over haemalum. Such slides are usually very fragmented, which makes the manual measurement of density particularly tedious and error-prone.

**Methods**

Our method starts with a precise determination of the zones of tissue on the whole-slide image. Then we measure their area and we calibrate automatically the staining optical densities and the background colour. Automated detection, measurement and counting of vessels takes place, based on a colour deconvolution [1] followed by automatic thresholding [4] and finally morphological operations to remove artefacts (e.g., dust). In order to deal with the large size of whole-slide images, many of which exceed the capacity of the computer’s memory, we proceed on rectangular extracts of the whole image. The whole treatment was performed on a standard desktop computer with 16 GiB of RAM [2]. In the end, masks of areas considered as tissue and as vessel walls and lumina are produced and uploaded, along with the virtual slide, to a webserver. This allows the pathologist to check the quality of segmentation from his office using a simple JavaScript-capable web browser. We tried two formats for web serving: DeepZoom (which can be served directly by a webserver) and pyramidal TIFF (which needs to be served by a modified version of IIJImage server [3] because lossless compression of the masks was used to preserve both disk space and image quality).

**Results**

Only a few parameters have to be chosen, once and for all samples (e.g., the minimal acceptable size of a blood vessel fragment), which makes the method more robust than assessment by a (panel of) human expert(s). The automatic calibration steps enable one to deal with a heterogeneous set of slides (e.g., slight differences in background colour and staining). The method uses only open-source software. It is easy to extend or improve and not tight to a single immunomarker.

We applied the method to 129 paediatric brain tumours of 8 different types and 3 locations (posterior fossa, thalamus, hemispheres) — 185 samples in total. For each patient, the density of microvessels in the sample is compared to the cerebral blood flow as assessed by preoperative perfusion–weighted-imaging using arterial-spin-labeling. We find a good correlation between microvascular density, MRI data and tumour grading. The microvascular density is broadly distributed among the samples.

Visualisation in a web browser is slightly more fluid when images are uploaded in the DeepZoom format rather
than as pyramidal TIFF images, but the former consumes roughly 20 times more disk space and needs the transfer of a very large number of files after each modification, which is less tractable.

Figure 1.

Figure 2.
Figure 3.

References: