Imaging the leptomeningeal paravascular space in humans and mice using Optical Coherence Tomography (OCT)

Material and methods

Human studies

The clinical procedures were carried out at the Radboud University (Nijmegen, the Netherlands) in accordance with the Declaration of Helsinki for experiments involving humans. From each patient, we obtained written informed consent. Privacy of the patients was ensured by anonymization.

Imaging of human and mouse paravascular spaces with Optical Coherence Tomography (OCT)

Human OCT data (n=5) were recorded using a commercial 50 kHz Santec IVS 2000 swept source OCT system operating at a center wavelength of ~1300 nm. The full width at half maximum (FWHM) axial and lateral resolutions were measured at ~14 µm and ~25µm, respectively. Volumetric images (x,y,z) of 10 mm by 10 mm by 4 mm, containing 1024 by 1024 by 600 pixels were collected from healthy brain tissue before tumor surgery, after craniotomy and the removal of the dura. The clinical procedures were carried out at the Radboud University (Nijmegen, the Netherlands) in accordance with the Declaration of Helsinki for experiments involving humans. From each patient, we obtained written informed consent. Privacy of the patients was ensured by anonymization.

Mouse OCT data (n=5) were recorded after preparing the thinned window as described in the method section of the manuscript. A commercial 100 kHz Santec IVS 2000 swept source OCT system was used, operating at a center wavelength of ~1060 nm. The FWHM axial and lateral resolutions were measured at 9 µm and 9 µm, respectively. The collected OCT images for both human and mouse were post processed to enhance image quality. Using FIJI software, two adjacent B scans were averaged to reduce the speckle prior to applying two filters (i.e. despeckle and sharpen) and enhancing the contrast. The depth axis of the OCT images were corrected for the refractive index (1.3) of mouse brain tissue.

Statistics

Linear regression analysis was done with Prism software (Graphpad).

Results

Prior to brain surgery, five patients were scanned with an OCT device across the brain surface. OCT images were taken from healthy sections of tissue. This showed the presence of numerous paravascular spaces next to blood vessels in all patients. A typical image is shown in Figure 1A. The technique does not allow discrimination between arteries and veins, nor does it provide data regarding flow in the paravascular space. However, it clearly showed paravascular spaces (PVS) across a range of vessel sizes, which appeared as widening of the subarachnoid space. The shadows beneath the vessels are an artifact of the technique. The size of the PVS was linearly related with the vessel size (Figure 1B). The morphology of the PVS was similar in mice (Figure 1C).

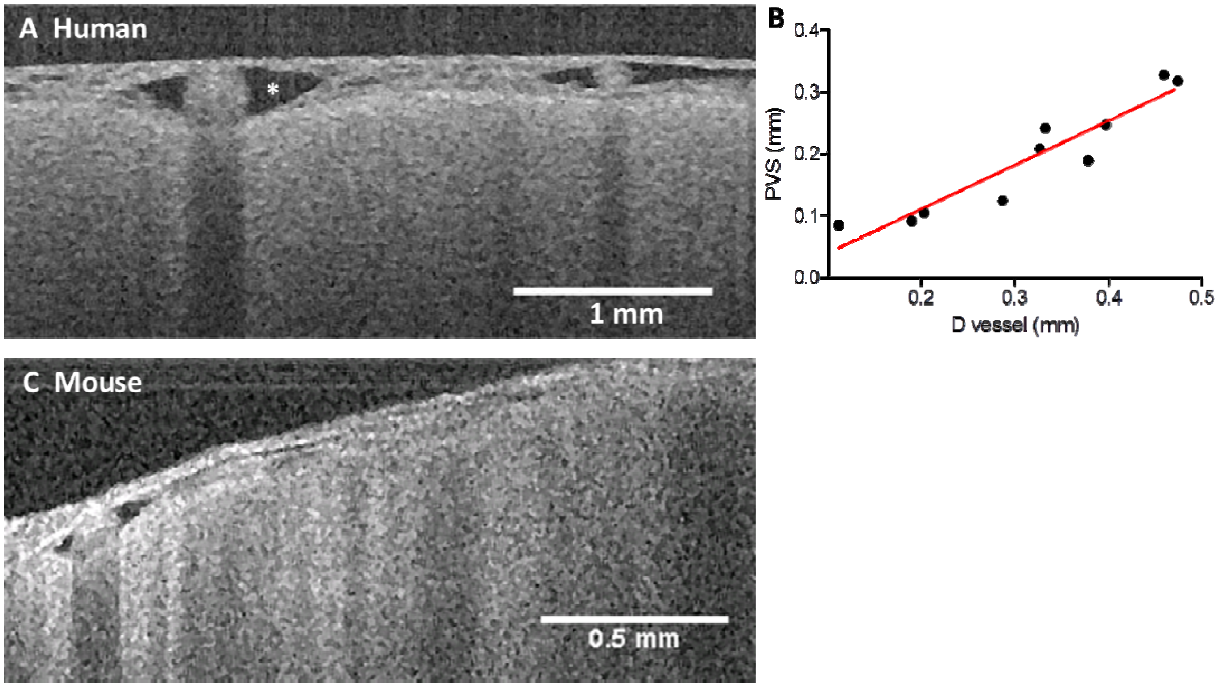

Figure 1. OCT imaging of human and mouse paravascular spaces. Panel A: human brain surface with paravascular spaces (*). Panel B: relationship between vessel diameter (D) and paravascular space size. Panel C: identical morphology of paravascular spaces at the surface of a mouse brain.

Video legend

Typical example of microsphere movement along a leptomeningeal vessel. Imaging through a thinned-skull cranial window shows the pulsatile nature of microsphere displacement. The microsphere moves in close proximity to the vessel. A capillary crosses the larger vessel. The arrow indicates the direction of blood flow.