

## **Intraoperative Imaging of Cerebral Vasculature and Blood Flow using Confocal Laser Endomicroscopy: New Perspectives in Precise Real-Time Brain Fluorescence Microimaging**

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### **Introduction**

Ability to assess the blood flow is a fundamental requisite in cerebrovascular surgery. Intraoperative fluorescent angiography with indocyanine green (ICG) and fluorescein sodium (FNa) under the operative microscope have become a standard procedure. However, such flow assessment is limited in number of attempts, duration and visible field of view. This is the first study to assess intraoperative confocal laser endomicroscopy for cerebral vascular imaging with FNa in a large animal model.

### **Methods**

Imaging was performed in-vivo on swine, rat and mouse brains after craniotomies using a new generation handheld confocal endomicroscope and an operative microscope. Confocal probe was positioned on the arteries, veins and brain tissue with a Greenberg retractor. Continuous images and Z-stacks were acquired after intravenous and intraarterial injections of FNa.

### **Results**

Blood flow was visualized in cerebral vessels of various sizes ranging from 7.2um to 1mm in diameter. Individual red blood cells and their movements were visible. Arteries and veins were discriminated based on the tortuosity and speed and pattern of flow. Changes in flow were readily visible after the vessel compression or proximal clip application. Overall, confocal angiography was possible for more than 40 minutes after a single 2mg/ml FNa administration, compared to about 6 min with the operative microscope. Multiple FNa reinjections (IA and IV) and co-administration of ICG did not decrease confocal image quality. Various intravascular events such as thrombosis, agglutination of erythrocytes, rolling of cells, redistribution/reconstitution of flow in a microvascular bed were visualized in a porcine brain.

### **Conclusions**

Confocal laser endomicroscopy is a novel technique that is capable of exquisite precision cellular-level imaging and blood flow assessment in cerebral vasculature on-the-fly during surgery. Confocal laser endomicroscopy extends imaging time compared to the wide field operative microscopy with FNa and provides additional details of intravascular cell movements.

### **Learning Objectives**

- Live confocal microscopy imaging allows visualization of blood flow in the cerebral vasculature for more than 30 minutes after fluorescein sodium injection.
- Blood flow was visible in vessels of various sizes, from 7 microns to 1 mm diameter.
- Various intravascular events could be visualized on a cellular level.
- Changes in the blood flow could be visualized after vessel compression or occlusion.

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