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Intraoperative imaging of the brain macro- and microcirculation

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Abstract

Advances in imaging technology have provided new diagnostic methods for assessment of cerebral vascular perfusion and quantitative analysis of the microcirculation during cerebral surgery. In this article, a range of imaging procedures are described: Digital Subtraction Angiography (DSA) and Three-Dimensional Computed Tomography Angiography (3D-CTA), Indocyanine Green Video Angiography (ICGVA), Orthogonal Polarization Spectral (OPS) Imaging, Sidestream Dark-Field (SDF) Imaging, and Laser-Doppler Flowmetry (LDF).

All these measurements will foster development of precise evaluation tools for microcirculation-related microvascular conditions, e. g. stroke and hemorrhage, and support clinicians in their therapeutic decision-making process.

Key words: angiography, cerebral surgery, intraoperative imaging, microcirculation, macrocirculation

Cerebrovascular surgery is an operative treatment for brain vasculature diseases, such as aneurysms, arteriovenous malformations, cavernomas, and occlusive vascular diseases like stroke. Traditionally, neurosurgeons directly inspect cerebral vessels with the aid of an operating microscope during surgery. To minimize the morbidity and mortality associated with the surgical treatment, angiography has been introduced and used as a standard method for preoperative diagnosis and postoperative evaluation of the vascular anatomy. However, if postoperative angiography reveals an abnormal surgical result, another surgical procedure has to be performed for correction or the compromised vessel has already caused an infarction. Therefore, intraoperative angiography has been applied for evaluating vascular anatomy and perfusion in real-time (1).

Maintaining the integrity of tissue perfusion through macrovasculature is one of the

basic principles of brain surgery, but maintaining the integrity of cerebral microcirculation is also critical and more challenging for function and survival of the tissue cells since supply of oxygen and nutrients to individual cells and elimination of waste products from cells occur in the microcirculation (2). However, imaging techniques for assessing microcirculation in clinical medicine, especially in brain surgery is very limited. In addition, there is a lack of agreement on which microcirculatory parameters and analyzing techniques can be used for evaluating the microcirculation. This makes the microcirculatory study more complex. The aim of this article is to review techniques of intraoperative imaging at macro- and microcirculation in human brain surgery.

Digital Subtraction Angiography (DSA) and Three-Dimensional Computed Tomography Angiography (3D-CTA)

DSA is considered as the “gold standard” for detection of cerebral aneurysms and monitoring surgical results intraoperatively or postoperatively (3). However, since it’s invasive, time-consuming and technical demanding, intraoperative DSA is not considered as a routine method for all the cases and not available in all the centers. 3D-CTA as another diagnostic method in the detection of intracranial aneurysms is found to provide comparable information to DSA, but less invasive, less time consuming, cheaper and easier to demonstrate the essential information regarding the aneurysm than DSA (4)(5).

Indocyanine Green Video Angiography (ICGVA)

ICGVA has been used in ophthalmology for many years but applied in brain surgery recently for intraoperative assessment of cerebral vasculature in routine or emergency surgery for patients with intracranial aneurysms (6), cerebral arteriovenous or dural fistulous malformations (7), moyamoya disease (8, 9) and decompressive craniectomy for malignant stroke (10). It was performed with a laser-fluorescence imaging device that consisted of a NIR laser light source (0.16 W, =780 nm) and a NIR-sensitive digital camcorder. The device was placed 30 to 40 cm from the area of interest and illuminated the area of interest with the laser light source. The NIR laser light emitted from the light source induced fluorescence of ICG, a NIR fluorescent dye injected intravenously. The fluorescence signal was recorded by the digital video camera with optical filtering to block ambient and laser light for collection of only ICG-induced fluorescence. Angiographic images could be reviewed on the

video screen in real time (25 images/s) and stored on the digital video camera or transferred to a computer (6).

ICGVA provides high quality image with spatial resolution that allows assessment of the arterial and venous vessels, including small arteries (<0.5 mm in diameter), and the visible aneurysm sac at real-time. It is a quick, reliable, cost-effective method and clinically useful in aneurysm, dural fistula, and revascularization surgery. It was reported that results obtained from intraoperative ICGVA in all the cases of aneurysms surgeries corresponded to the postoperative angiographic finding, but in some cases, the information provided by intraoperative ICGVA significantly changed the surgical procedure (6). The major limitation of the method was that the ICG angiographic views were restricted to the angle of the surgical approach. Vessels that were covered by blood clots or aneurysm or brain tissue could not be observed with this technique (6).

In a recent study, Schnell and co-authors compared advantages and drawbacks of ICGVA and intraoperative computed tomography angiography (iCTA) and intraoperative computed perfusion tomography (iCTP) on visualizing brain vasculature during aneurysm surgery (11). They found that ICGVA was able to detect blood flow and vascular patency in the vessels only located in the visual field of microscope but not in the deeper areas of surgical field. iCTA provided high quality image in 7/10 patients but could not detect small arteries. iCTP was also able to detect global blood flow in some cases but not in others. Therefore, ICGVA and iCTA/iCTP are complementary rather than competing techniques and able to assess local and regional blood flow and cerebral perfusion in intracranial aneurysm surgery (11).

Orthogonal Polarization Spectral (OPS) Imaging

OPS imaging is a noninvasive method for assessing microcirculation on the surfaces of organs. It uses a handheld device with a small optical probe. The tissue is illuminated with linearly polarized light and only depolarized photons scattered from the tissue contribute to the imaging (12). It produces high contrast microvascular images that allow viewing and quantifying microcirculatory hemodynamic changes at real-time and provides a convenient method for intravital microscopy on the brain surface.

OPS has been used to assess cerebral microcirculatory changes during brain surgeries of arteriovenous malformation (AVM) (13), aneurysm (14)(15) and tumor removal (16). Parameters of microcirculation, including diameters of blood vessels, microvascular flow index (MFI), functional capillary index (FCD), flow kinetics and arteriolar contractility could be evaluated during the surgeries. For example, in AVM surgery, Pennings and coauthors demonstrated that prior to AVM excision, cardiac pulsation was absent in the arterioles and individual erythrocytes were observed due to the slowing of blood flow. However, increased flow velocity (to a level that individual erythrocytes could not be traced), FCD and MFI were observed after resection (13). In brain tumor surgeries, stop-flow and spurt-flow with irregularly shaped vessels and large mean vessel diameters were observed in tumor microcirculation in comparison to normal healthy cortex, which always expressed continuous flow (16).

Although OPS imaging greatly contributes to study the brain microcirculation, there are still weaknesses by using OPS imaging such as motion-induced image blurring caused by movement of the OPS device, the tissue and the blood flowing. In addition, it is difficult to measure flow velocity in large vessels, especially during continuous flow, due to blurring of images (17, 18).

Sidestream Dark-Field (SDF) Imaging

SDF imaging is another noninvasive technique for continuous observation of cerebral microcirculation on the brain surface during brain surgery. It is a further development of OPS techniques and consists of a handheld videomicroscope containing a ring of stroboscopic light emitting diodes (18). Using SDF, Perez-Barcena and coauthors reported direct visualization of blood flow and vessel density of cerebral microcirculation in patients who underwent decompressive craniectomy after infarction of cerebral artery and the non-stroke control patients who underwent craniotomy for diseases other than stroke (19). The cortical vessels in the control patients were regularly shaped with continuous blood flow in all sizes of vessels (from 10 to 100 μm in diameters) and the proportion of the perfused vessels was near 100%. The cortical vessels in the patients with stroke showed intermittent or no flow with smaller proportion of perfused vessels (63.44%). The perfused vessels density index was also higher in control group than in patients with stroke (19).

However, SDF imaging cannot directly measure the velocity of erythrocytes since high erythrocyte velocity exceeds the capture rate of the camera for tracing individual red blood cells. In addition, pressure-induced microcirculatory alterations caused by application of the SDF probe onto the tissue surface might lead to false interpretation of actual microcirculation perfusion (18, 19). In the future, new devices with more advanced camera technology may solve the problem for measuring the velocity of erythrocytes.

Laser-Doppler Flowmetry (LDF) and Combined With Photospectrometry

Laser Doppler flowmetry (LDF) was established as a noninvasive method for continuous and real-time measurement of blood

flow in the microcirculation. It measures relative microcirculatory flow based on the Doppler shift of the illuminated laser light caused by the movement of red blood cells (20). The light is able to penetrate into the depth of tissue and measure microvascular blood flow throughout it, but the depth depends on optical feature, wavelength used and the diameter of the beam (21). LDF has been used in the intraoperative assessment of cortical blood flow during general neurosurgical procedures (22) and surgeries for cerebral arteriovenous malformations (23) and various cerebral tumours (24). The major disadvantage is its high sensitivity to motion-produced disturbances.

Recently, a novel monitoring device (O2C, oxygen-to-see device) based on combined laser-Doppler flowmetry and photo-spectrometry has been introduced to monitor cortical microcirculation during intracranial surgery (25-27). The device consists of a computer with built-in laser and light emitting diodes and a fiber optic measurement probe. It transmits continuous wave laser light (830nm) and white light (500-800nm) to tissue and collocate the scattered light from tissue to the probe. The Doppler shift of the illuminated laser light is displayed as blood flow velocity while the collected white light is split into its spectral components and converted into an electrical signal. Oxygen saturation is determined by comparison with prerecorded deoxygenated and oxygenated hemoglobin spectra, while the tissue hemoglobin values are determined by the amount of light absorbed by the tissue. This device is used only for measurements in the microcirculation (<100 μm diameter) since light from bigger vessels (> 100 μm diameter) is completely absorbed (26, 27). Relative blood flow is calculated based on the product of moving erythrocytes and velocity of each erythrocyte.

This device is able to determine regional capillary-venous cerebral blood flow, oxygen saturation and hemoglobin amount simultaneously in the cortical/cerebral tissue. It is easy to set up and can be used continu-

ously during brain surgery. Although the depth of measurement is dependent on the distant between the illuminating and detecting elements, the type of probe used and optical characteristics of the tissue, it has been used for measuring cerebral microcirculation from 2 mm to 8 mm of depth. However, this device only provides relative values, not quantitative measurement due to the feature of laser-Doppler flowmetry. In addition, the measurement may be influenced by neurosurgery, cortical temperature and blood film in the cerebral cortex (26, 27).

In conclusion, advances in imaging technology provide new diagnostic methods for assessment of cerebral vasculature perfusion and quantitative analysis of the microcirculation during cerebral surgery. The measurements will be essential in developing precise tools to evaluate microvascular conditions that may affect the microcirculation, such as stroke or hemorrhage and contribute to the further therapeutic intervention.

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