Superselective Intracerebral Catheterization of a Branch of the Internal Carotid Artery Coupled with Magnetic Resonance Imaging

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Summary

We used fluoroscopic guidance and over-the-wire techniques to superselectively place a microcatheter into a branch of the MCA of three macaques and MRI bolus tracking techniques to measure perfusion within the selected brain region. Such techniques are likely to be useful in the assessment and treatment of ischemic infarction, cerebral vasospasm, and monitoring local delivery of drugs into the brain.

Introduction

Vascular interventional procedures are minimally invasive image guided techniques typically involving antegrade superselective catheterization (SSC) of blood vessels. Superselective catheterization has found application in the following clinical and research areas: in humans, preoperative embolization of body and brain tumors¹⁻⁶, intraarterial (IA) administration of thrombolytic agents⁷⁻⁹ as well as to treat arteriovenous malformations and aneurysms^{10,11}. In addition, in animal models, SSC has been used to create strokes in non-human primates¹²⁻¹⁴. Recent improvements in transaxial imaging modalities, computed tomography and magnetic resonance angiography have led to significant improvements in the evaluation of

cerebral vascular anatomy without requiring invasive studies. CT and MR have the additional benefits of displaying precise anatomic data as well as functional and perfusion data.

The current "gold standard" for visualization of the cerebral vascular anatomy in neurointerventional procedures is digital subtraction angiography. While this technique allows real time visualization of neurovascular structures sufficient to guide interventions within the cerebral vessels, ideally it would be advantageous to have precise neuroanatomic details as well as physiologic and functional data immediately prior to, during and following intervention and treatment. There have been some developments in combined MR/X-ray systems as well as neurointerventional tools for image guided interventions¹⁵⁻¹⁸ however, non-magnetic catheters/guide wire combinations for neurointerventions, i.e., in the brain, are not adequately developed at present.

The purpose of this study was to demonstrate the feasibility of obtaining local parenchymal tissue perfusion information using a standard microcatheter and interventional technique. We report the first use of in vivo magnetic resonance imaging to monitor the ICA arterial territory which was superselected using an MRI compatible microcatheter in nonhuman primates.

Methods

Experimental Animals

Adult male cynomolgous macaques (*Macaca fascicularis*, $n=3$, 8.5 ± 0.6 kg) were used to evaluate the method. These preliminary studies were done to investigate whether it was feasible to create smaller branch MCAO strokes which would be more survivable than MCAO trunk occlusion strokes. All animal procedures were approved by the animal care panels at our institution. Animals were anesthetized with Propofol (300 $\mu\text{g/kg/hr}$) and Remifentanyl (0.1 $\mu\text{g/kg/hr}$) and placed supine in an MRI compatible holder. Animals were intubated and mechanically ventilated with a 20/80% oxygen/air mixture, to keep end tidal CO_2 between 30-40 mmHg. An incision was made in the femoral groove, the femoral artery isolated and cannulated with a 5.0 French pediatric vascular sheath. Heparin (IV bolus of 500 units) was given, just prior to the start of the interventional procedures, to prevent clotting in and around the catheters. A single dose of Verapamil (0.05 mg/kg, IV) was infused slowly to minimize vasospasm (directly after the surgical cutdown procedure and at least half an hour in advance of the start of the interventional procedures). Lactated ringers solution was given at the rate of 10 ml/kg/h to maintain hemodynamic stability.

Figure 1 Lateral X-ray of the primate's head showing the position of the guide catheter in the CCA (solid white arrow) and microcatheter tip in the MCA branch (dashed white arrow).

Endovascular Approach

Under X-ray fluoroscopic guidance (Siemens Hicor, Siemens Medical Systems), a 5 French Envoy[®] guiding catheter (Cordis Corp, Miami Lakes, Florida USA) was introduced over a TerumoTM 0.038" angled guidewire into the arterial sheath and navigated under fluoroscopy via the proximal aorta into one common carotid artery. This catheter was positioned in the common carotid artery (CCA) in close proximity to the internal carotid artery (ICA) (approximately 5 mm proximal to the CCA/ICA bifurcation). A cerebral angiogram was performed by injection of iodinated contrast media (Monegasque, Amersham Health, USA) through the guiding catheter to view the cerebral vascular anatomy in preparation for the introduction of the microcatheter. A 1.7 French (0.55 mm o.d.) microcatheter (Prowler-10TM; Cordis Neurovascular Inc, Miami, Florida, USA) was introduced through the guide catheter over an Agility-10TM soft microguidewire (Cordis Neurovascular Inc, Miami, Florida, USA). This microcatheter was specifically chosen because the last 50 cm up to the tip is unreinforced and is non-magnetic. In combination with the microguidewire, the microcatheter was transarterially navigated to superselectively catheterize a branch of the middle cerebral artery (MCA) positioned just shy of occluding the vessel, and the position verified by digital subtraction angiography. The guidewire was then removed and both the microcatheter and guide catheter were secured on the leg using Tegaderm (3M Healthcare, Borken, Germany).

MRI

After the catheters were secured, the animals were moved immediately to the adjacent 1.5T MRI scanner while still under anesthesia (on average the transfer took 15 minutes). Conventional spin-echo MRI was used for acquiring anatomical images, from which 10 axial slices were prescribed for perfusion-weighted imaging. Perfusion weighted imaging (PWI) of the entire brain was performed during the passage of a 1.0 ml bolus injection of contrast agent, GdDTPA (Magnevist, Berlex Labs., Richmond, CA) (0.01 mmol), which was delivered in one to two seconds through the microcatheter. We used a single shot gradient-echo EPI (TR 3s, TE 70 ms, 12 cm FOV, 64 x 64 matrix, 2.5mm slice thickness) sequence to track the bolus. Image data were analyzed using MRVision software

(MRVision Co., Winchester, MA). PWI were processed to generate maps of time-to-bolus peak (TTP- the delay between the start of the scan and the peak of the signal change caused by the bolus passage through the tissue and relative cerebral blood flow (rCBF).

Results

All animals tolerated the surgical procedure, angiography and MRI well. Although the distal end of the microinfusion catheter is nonmagnetic, the guide catheter is reinforced and is slightly magnetic. This can produce severe image distortions in the EPI scans, if positioned too close to the brain. However with the guide catheter positioned in the CCA (figure 1) no image distortions were seen (figure 2A). Figure 2B,C shows the hemodynamic maps calculated after contrast agent injection. The "time-to-peak" maps (figure 2B) show the relative variation in bolus arrival throughout the brain, with earlier arrival closer to the MCA, while the rCBF maps (figure 2C) highlight the vascular territory perfused by the MCA downstream from the point at which the microcatheter tip was positioned. rCBF maps from another animal are shown in figure 2D, which demonstrates a much smaller region of enhancement, consistent with a more distal position of the microcatheter tip.

Discussion

Digital subtraction angiography is the method of choice for many diagnostic vascular imaging procedures as well as for monitoring endovascular interventions. Neurointerventional techniques have steadily improved, but a significant limitation to endovascular neurosurgical techniques is the reliance predominantly on the vascular anatomy for guidance. While digital subtraction techniques allow for unprecedented resolution of vascular anatomy, they do not allow precise imaging of brain parenchyma or provide functional data. Ideally, one would prefer to precisely visualize both normal and abnormal tissue in the immediate vicinity of the proposed neurointerventional procedure and observe functional data in real time. We describe our experience using local PWI to monitor injections of MRI contrast agent in the normal brains of primates. We were able to observe vascular (the passage of a bolus of MR contrast agent) and parenchymal response

Figure 2 Hemodynamic maps from microcatheter injection of Gd-DTPA. A) Baseline multislice EPI images. B) Time-to-peak: darker pixels indicate an earlier bolus arrival time (white mottled area is noise in tissue not perfused by the microcatheter). C) Relative blood flow (rCBF), indicating the territory perfused by the vessel containing the microcatheter. D) rCBF maps from another animal in which a much smaller volume of brain tissue was perfused from the microcatheter in the MCA.

within seconds. In our case, animals were transported rapidly between the fluoroscopy unit and the adjacent MRI scanner. With the advent of the combined interventional X-ray/MRI systems (18), transport time between angiography and MRI can be minimized.

One can imagine cases where this combined fluoroscopy/MRI perfusion approach may prove important in clinical practice. For example, MR intra-arterial contrast enhanced evaluation will be useful for monitoring brain tissue affected by a thromboembolus which has been

treated with intra-arterial thrombolytics. The procedure could be terminated if all eloquent tissue is perfused, to lessen the amount of thrombolytic agent given and the risk of bleeding, or the efforts could be redirected if certain eloquent tissue remained unperfused. The intra-arterial dose of MR contrast used is very low, so that multiple boluses can be given during the course of the intervention. In addition, the MR soft tissue anatomy of both the involved and the contralateral brain tissue can also be evaluated at the same time (e.g., using diffusion weighted MRI). Other examples include precise demonstration of the brain region perfused to enhance interpretation of superselective temporary pharmacologic-physiologic ablation, since one would have demonstrable proof that the anatomic area of interest was perfused with the medication injected. Local parenchymal information would also be useful for evaluating the efficiency of blood brain barrier disruption prior to intra-arterial chemotherapy infusion.

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Conclusions

The use of the MR compatible Prowler 10 with its unreinforced tip allowed superselective branch MCA catheterization and artifact free MRI of the selected arterial territory with the catheter in-situ. The techniques and catheters used in this report are already in use clinically and intervention followed by direct focal treatment of brain tissue under MR observation is certainly possible in the human brain. The techniques described here can be easily translated into medical use if appropriate equipment is available and safety procedures are in place.

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