Material Requirements for Therapeutic Embolization of Intracranial Vascular Malformations

The last of a three-part series on diagnosing, treating, and researching management options for intracranial malformations.

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Definitive treatment of vascular malformations often requires surgery or radiosurgery. Various embolization techniques, however, have come to enhance and, sometimes, replace surgical methods by occluding the lesions.[1-5] Current trends in research are focused on refining imaging modalities to identify lesions earlier, to allow for close monitoring and risk stratification. In therapeutics, liquid embolics are being adapted to accommodate cerebrovascular anatomy and minimize unnecessary ischemic damage to neural tissue. Customization of catheters used in delivery of these embolics is also concurrently being done to optimize delivery. In the final section of this series, we elaborate on these developments in the management of cerebrovascular malformations.

TECHNOLOGIES IN RESEARCH

Imaging Modalities

Collaborative efforts among researchers in neurosurgery, radiosurgery, vascular surgery, and neurology have significantly advanced our understanding of neuroendovascular intervention, particularly for arteriovenous malformations (AVMs), dural arteriovenous fistulas, and tumors. Imaging modalities such as CT scans and magnetic resonance imaging (MRI) continue to be highly utilized in detection and treatment of AVMs. The introduction of noninvasive and highly sensitive neuroimaging devices such as MRI and CT angiography have resulted in earlier detection of unruptured cerebral lesions in patients and provides valuable information such as the topography and localization of an AVM.[6,7] Through early detection, the morbidity and mortality associated with hemorrhage and stroke can be reduced. Vascularization of tumors and sites of rupture are assessed via angiography of the vessels, specifically neurovascular digital subtraction angiography and magnetic resonance angiography. Currently, it is highly recommended to obtain an MRI study and a four-vessel angiogram to examine the course and features of an AVM.[7]

Embolic Materials

The testing of new embolic agents, performed only in animal models in the past, is continuously being translated into the clinical setting. In general, the field has seen the development of novel materials that precipi-

tate or augment blood coagulation and were initially tested in a variety of in vitro models.[8,9] Typically, material characterization with rheology, microcatheter delivery, radiopacity, and cytocompatibility precede in vitro hemocompatibility evaluation.[9-11] Subsequent to demonstration of safety in vitro, materials are then evaluated in simple embolization models to show occlusive potential. These include embolization of rabbit kidneys, swine rete mirabilia, and even creation of saccular aneurysms from adjacent vasculature.[12-16] The first-in-human clinical trials that typically followed identified a select number of potential materials that have suitable flow and catheter delivery characteristics, suitable carrier/solvent systems that cause minimal toxicity, and safety with minimal nontarget side effects.[17-22]

Adjunct Technologies

Adjunct technologies have augmented the use and delivery of liquid embolics. For example, there have been major advances in catheter technology to aid in material delivery.[23-29] Early microcatheters were unbraided and prone to distortion as they passed around sharp curves. Braided microcatheters with hydrophilic coatings were subsequently developed to increase tracking ability and convey resistance.[30] Flow-directed microcatheters, which are braided except at the tip, have been invaluable for embolization of AVMs in the brain because they can advance into long feeders toward the site of embolization.[31] However, the flow-directed catheters are limited by which embolic agents, particularly coils, can pass due to size restrictions.[32] Microwires have similarly been optimized for use in embolization procedures.[33] Catheter cerebral arteriography is commonly used to confirm the presence, size, and location of intracranial aneurysms.[34] However, the wide variation in clinical presentation and low incidence of AVMs has been a major obstacle in developing diagnostic and therapeutic modalities.

Future Directions

From a materials and surgical perspective, achieving high biocompatibility and low immunogenicity of materials is imperative in the design of next-generation materials.[35,36] An understanding of the human tissue response to embolization is essential in the development of successful embolic materials. Several liquid embolic agents that use a carrier solvent such as dimethyl sulfoxide, which is displaced to allow precipitation of the material, cause vasospasm, acute cytotoxicity, and potential necrosis.[28,37-40] However, much is still unknown about in vivo reactions to embolic agents, including long-term consequences for both AVMs and various tumors.[28,41] The delicate balance that is maintained between sufficient embolization to prevent recanalization and overfilling to prevent inadvertent end-organ embolization is a constant challenge.[42] Although these therapeutic modalities have come a long way, the full benefit can only be extracted through increased collaborative efforts between the material scientists and surgeons.

CONCLUSION

This final article of a three-part series on cerebral AVMs and dural arteriovenous fistulas aimed to summarize the technologies under development and what novel therapies are being developed. With technological advances, further interdisciplinary collaboration between material scientists, physicians, and surgical specialists will pave the way for clinical applicability and ultimately improve patient outcomes. This concludes a review on our understanding of cerebrovascular lesions, current treatment paradigms, and anticipated developments in research. ■

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