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Hydrophilic Coatings Diminish Adhesion of Glue to Catheter: An In Vitro Simulation of NBCA Embolization

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PURPOSE: To determine whether new hydrophilic microcatheter coatings exhibit characteristics that diminish the chance of permanent endovascular glue adhesion during liquid acrylic embolization. **METHODS:** Common hydrophilic and nonhydrophilic microcatheters (both flow-directed and over-the-wire) used in neurointerventional procedures were evaluated in vitro for liquid acrylic (Histoacryl and Avacryl)–to–catheter bond strength, catheter endovascular friction, and catheter stretch (tensile strength). Sufficient test repetitions were acquired to achieve statistical significance. **RESULTS:** The bond strength between hydrophilically coated catheters and NBCA was significantly weaker than between nonhydrophilic catheters and NBCA. Hydrophilic catheter coating reduced dynamic endovascular friction by 30% to 35%. All flow-directed catheters exhibited considerably more stretch (less tensile strength) and therefore were more prone to fracture during withdrawal than over-the-wire systems. Histoacryl bonded to both hydrophilic and nonhydrophilic catheters with a significantly greater force than did Avacryl. **CONCLUSION:** Hydrophilically coated catheters should be less likely to exhibit permanent endovascular fixation during acrylic embolization because of a weaker catheter-NBCA bond and because of reduced catheter friction (allowing a larger portion of any applied catheter withdrawal force to be transmitted to the catheter tip with less force dissipated along the catheter resulting in stretch). A significant difference in NBCA types (Histoacryl and Avacryl) was discovered: Avacryl developed a significantly weaker bond with all catheter types.

Index terms: Interventional materials, cyanoacrylate; Catheters and catheterization, instruments

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Cyanoacrylate tissue adhesives have been in clinical endovascular use since the 1970s (1). Original clinical experience was gained with a vinyl monomer of the alkyl 2-cyanoacrylates, isobutyl 2-cyanoacrylate (IBCA) (1–7). This agent became unavailable by the late 1980s and was replaced by a similar compound, *N*-butyl 2-cyanoacrylate (NBCA) (8–10). At present, NBCA can be obtained only under the name Histoacryl (B. Braun, Melsungen, Germany). A similar preparation was marketed under the name Avacryl (Tripoint Medical, Raleigh, NC) but was withdrawn from medical use in 1992.

Liquid acrylics are extremely useful as endovascular embolic agents because of their ability to create permanent vascular occlusion (6, 7, 11–19). They may, however, be difficult to use technically as they have a variable and sometimes unpredictable polymerization time based on the operator selection of an acrylic mix with either iodinated oil or glacial acetic acid (8, 20, 21). The appropriate choice of polymerization time depends on a number of variables, including the transit time between arterial and venous elements in the embolic target, the target volume, the architecture of the target (fistula ver-

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sus nidus), which affects the relative endovascular turbulence, and the method of injection (bolus, full column, or wedge-flow arrest) (19, 22). Complications associated with the use of liquid acrylics for embolization occur when there is occlusion of normal arterial branches or acrylic penetration into critical venous outflow channels. Additionally, reflux of acrylic around the delivery catheter tip can result in permanent endovascular catheter adhesion, which may require permanent catheter implantation. Overzealous attempts at withdrawal can produce catheter fracture (and resultant embolization of a flow-directable distal catheter segment), vascular damage with resultant dissection/occlusion, or avulsion of the involved vascular pedicle (with resultant subarachnoid hemorrhage).

It was our belief that the development and availability of new hydrophilic catheter coatings might reduce the risk of inadvertent endovascular catheter fixation during embolization due to reduced bond strength between the hydrophilically coated catheter and NBCA. We describe an in vitro experiment that explores this hypothesis by attempting to determine the relative bond strength between NBCA and several microcatheters used for neurointerventional procedures. Additional catheter characteristics evaluated include tensile strength (which is inversely related to the catheter's propensity to fracture during withdrawal) and endovascular sliding fraction.

Materials and Methods

The following catheters were used: Fastracker 18 (Target Therapeutics, Fremont, Calif), Tracker 18 (Target Therapeutics), Zephyr (Target Therapeutics), Faszephyr (ZIII) (Target Therapeutics), and Magic 1.8 (Balt, Montmorency, France).

In the first portion of our experiment, we compared the bonding strength of Histoacryl liquid acrylic (NBCA) with each of the catheters just named. The terminal 1-cm segment of the distal portion of each catheter was placed in a 1-cm-deep well that was subsequently filled with human serum. The serum was displaced by a volume of NBCA (1 mL NBCA to 0.2 mL ethiodized oil) that exactly filled the well. (This NBCA–ethiodized oil combination was chosen to get a "fast" polymerization mix, which produces a stronger glue-catheter bond than does a "slower" mix that incorporates a larger proportion of ethiodized oil.) A 1-minute polymerization time at room temperature elapsed before the catheter was withdrawn from the glue plug. Digital computerized data measuring the force required to break the glue-catheter bond and the catheter stretch during pullout were obtained with a Tinius Olsen Locap Universal Materials Testing Machine (Tinius Olsen, Willow Grove, Pa). The linear variable displacement (stretch) transducer (serial #163950) had a resolution of 0.0001 inches. The load (force) transducer (serial #209135) had a resolution of 0.0001 lbs.

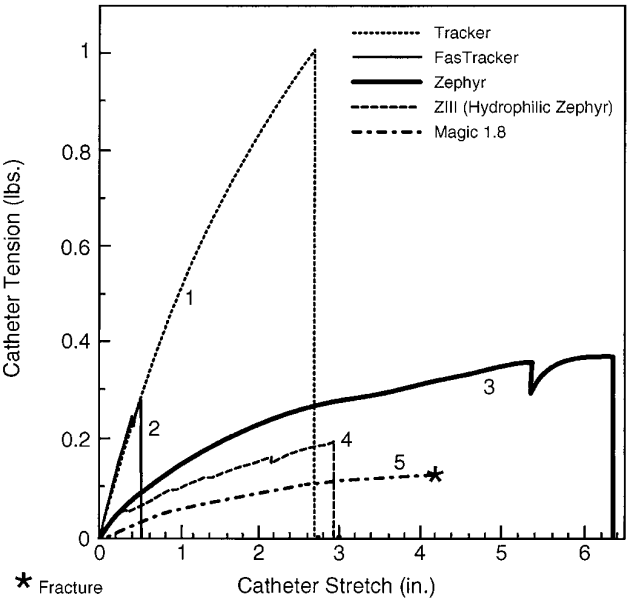

Fig 1. A representative catheter extraction curve for each catheter type is shown. Hydrophilic catheters (*2, 4*) detached from the NBCA bond with less force than did their respective nonhydrophilic catheters (*1, 3*). Flow-directed catheters (*3, 4, 5*) showed more stretch/unit force than did over-the-wire catheters (*1, 2*). The Magic (*5*) fractured rather than pulling out of the NBCA bond in this in vitro test situation.

Each group of catheters was withdrawn from the acrylic five times (Fig 1). There was a wide intergroup variation in results. It was obvious that differences in catheter behavior (force required to pull the catheter out of the acrylic plug and associated catheter stretch) was in part related to physical differences in the catheters other than simply bond strength between the catheter and NBCA. To minimize these variables, short (3-cm) tip segments of similar (Tracker and Fastracker) catheters were pulled using the same apparatus except the well depth was changed to 5 mm. This eliminated stretch as a major variable and allowed a comparison of similarly constructed catheters with and without hydrophilic coatings. This was accomplished 10 times for each catheter type with both Histoacryl and Avacryl (Table 1). Mean force and standard deviation were calculated for each catheter-glue combination. Hydrophilic and nonhydrophilic data were compared using Student's *t* test to assess significance between these groups.

Additionally, catheter friction was measured for each catheter type using a device that simulated an intravascular situation. The experimental setup placed each catheter through a fixed number of simulated vascular loops. All points at which the catheter contacted the "vascular surface" were covered with freshly harvested pig aorta and suspended in a saline bath. A known weight was fixed to

TABLE 1: Mean force required to extract hydrophilic and nonhydrophilic catheter segments from NBCA (both Histoacryl and Avacryl)

Catheter	Glue	Mean Force, lbs	Standard Deviation	No. of Extractions
Tracker 18	Histoacryl	1.01	.15	10
Fastracker 18	Histoacryl	.34	.13	10
Tracker 18	Avacryl	.58	.22	10
Fastracker 18	Avacryl	.23	.08	10

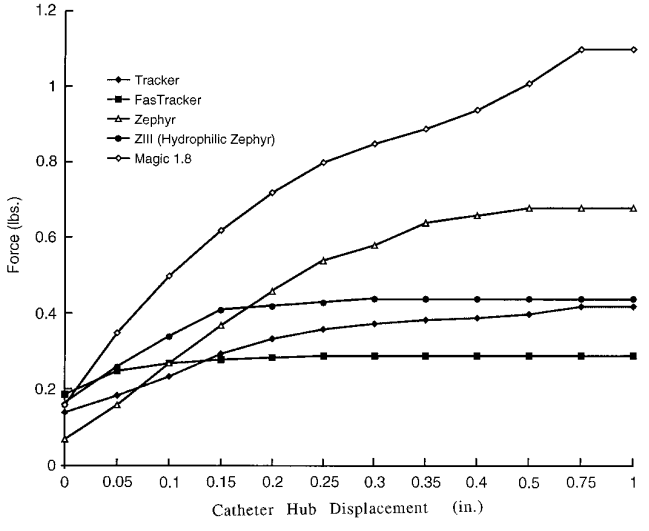

Fig 2. Representative friction tests indicate a lower dynamic friction for hydrophilic catheters (Fastracker and Faszephyr-III) relative to their nonhydrophilic counterparts (Tracker and Zephyr). All flow-directed systems exhibited higher intrinsic friction than the over-the-wire catheters and therefore required more withdrawal force at the catheter hub to effect catheter movement.

the distal catheter tip through a pulley arrangement and the force required to withdraw the catheter measured with the Tinius Olsen Materials Testing Device. The measured force at the catheter hub required to begin catheter withdrawal (F_W) was equal to the known weight attached to the catheter tip (W) and the force lost in the system to friction (F_F).

$$F_W = W + F_F$$

Three test measurements were obtained for each catheter type and the results were averaged (Fig 2).

Results

Initial tests (using the entire catheter) showed that hydrophilic catheters tended to pull out of NBCA with less force than did nonhydrophilic catheters (Fig 1). Both hydrophilic and nonhydrophilic catheters could be extracted from NBCA (in this nonphysiological, zero-friction setup) with the exception of the Magic, which uniformly fractured after considerable stretch. However, material differences between the catheter types (wire-directed versus flow-directed) revealed a wide range of results, with flow-directed catheters exhibiting considerably more stretch during withdrawal than the wire-directed variety (Fig 1).

TABLE 2: Mean force (measured at the catheter hub) required to produce steady catheter withdrawal during in vitro friction testing (three extractions for each catheter group)

Catheter	Mean Force, lbs	Standard Deviation
Tracker 18	.42	.03
Fastracker 18	.29	.012
Zephyr	.68	.035
Hydrophilic Zephyr (Z-111)	.44	.055
Magic 1.8	1.1	.13

In an attempt to reduce such physical variables as catheter stretch, short catheter tip segments (from one basic catheter type only) were withdrawn from the NBCA. Tip segments of Tracker and Fastracker catheters were withdrawn from Histoacryl and Avacryl. A statistically significant difference between hydrophilic and nonhydrophilic bond strength was demonstrated at the $P = .001$ level (Table 1). In both situations, the hydrophilic Fastracker segments released from the NBCA plugs with less force. Interestingly, it was found that Histoacryl bonded to both hydrophilic and nonhydrophilic catheters with a greater force than Avacryl did. This bonding difference was also found to be statistically significant at the $P = .001$ level.

Simulated intravascular sliding (dynamic) friction for each catheter revealed that hydrophilic coatings reduced friction by 30% to 35% compared with nonhydrophilic coatings (Table 2). All flow-directed catheters in this test exhibited more friction than over-the-wire catheters, even though friction was reduced by adding a hydrophilic coating (Fig 2). The greatest amount of friction was associated with the

Magic (a flow-directed catheter composed of polyvinylchloride).

Discussion

At least two decades of experience has now been accumulated with direct and endovascular therapeutic embolization of arteriovenous malformations with liquid acrylics (6, 7, 11–19, 22). Early modifications in the polymerization time and radiopacity of embolized mixtures of liquid acrylic have afforded more embolic control and improved the safety of the embolization procedures. Polymerization times are adjustable by the addition of iodinated oils (Ethiodol, Savage Laboratories, Melville, NY, or Pantopaque, Lafayette Pharmacal, Lafayette, Ind) or glacial acetic acid (8, 20, 21). By using these agents, polymerization times ranging from 0.2 to 5 seconds may be achieved. However, a potential complication of the endovascular use of liquid acrylics has always been the possibility of permanently gluing a delivery catheter into the vessel being embolized (23, 24). With careful attention to detail, this complication can be largely avoided by stopping the embolization and withdrawing the delivery catheter when the polymerizing glue column approaches the catheter tip. Even so, catheters are occasionally glued into vessels and have to be permanently implanted. The advent of hydrophilically coated microcatheters has suggested the possibility that the risk of permanent catheter adhesion during embolization might be decreased.

The proprietary hydrophilic coating used on the Fastracker and Faszephyr (ZIII) is Hydrolene (Target Therapeutics). A variety of microcatheters commonly used in interventional neuroradiologic procedures were surface-modified by chemically bonding this hydrophilic polymer, which is composed of polyvinylpyrrolidone and polyacrylamide. The Hydrolene coating is approximately 2 μm thick.

Our findings indicated that a weaker glue-catheter bond forms between NBCA and Hydrolene than with nonhydrophilically coated catheter materials. The safety improvement achieved by the primary reduction in NBCA-Hydrolene bond strength is enhanced by the coexistent reduction in endovascular friction of the hydrophilic catheters. The friction reduction of the hydrophilic systems serves to transmit to the catheter tip a greater proportion of the force applied when the catheter is withdrawn. The force (F_{tip}) delivered to the catheter-NBCA bond is equal to the primary pull force (F_{pull}) at the catheter hub minus the force lost to friction and stretch.

$$F_{tip} = F_{pull} - \text{friction}$$

A weaker glue-catheter bond results in a smaller pullout force and reduces the tensile strain on the catheter during pullout, diminishing stretch and decreasing the risk of catheter fracture.

Because catheter delivery systems have a finite tensile strength, they will tolerate only a limited applied tensile force before fracture occurs. The spectrum of tensile strength of the catheters under test revealed that over-the-wire systems (Fastracker and Tracker) are more rigid than the flow-directed type (Zephyr and Magic) and thereby exhibit less catheter stretch during withdrawal. Over-the-wire systems were consistently withdrawn from the glue-catheter bond without fracture. Flow-directed systems, by design, exhibit much less tensile strength, have greater stretch per unit length, and are more prone to fracture during withdrawal. In this in vitro experiment, the Magic consistently fractured before breaking the glue-catheter bond. The Zephyr and Faszephyr (ZIII) showed less tendency to fracture or to be permanently glued in than did the Magic. The Zephyr fractured 40% of the time whereas no fractures were seen with the Faszephyr. These catheters have an intermediate amount of stretch (less than the Magic but more than over-the-wire systems).

The findings with both Histoacryl and Avacryl in this experiment indicated that different NBCA preparations may have decidedly different bonding characteristics. Avacryl (presently not available in the United States for human use) had a statistically lower ($P = .001$) bond strength with both hydrophilic and nonhydrophilic catheters. If available, this material would also decrease the likelihood of permanent catheter adherence during acrylic embolization.

The actual risk of permanent endovascular catheter fixation during acrylic embolization is not known. It varies with operator proficiency, type of embolization, mixture of glue with polymerization retardants, and catheter type. This technical problem is usually not associated with a clinical neurologic complication unless there is fracture of the distal catheter (which can allow antegrade blood flow to accordion the residual catheter segment and produce a proximal vascular occlusion); spasm; damage to the intima,

causing dissection or occlusion; or rupture of a vascular pedicle during attempted withdrawal. When catheter adhesion occurs despite an accurately coordinated and graded withdrawal attempt, endovascular implantation should be performed. An animal study (using a 1F polyethylene catheter) has revealed no detectable untoward local endovascular reaction or significant increase in embolic risk with long-term endovascular implantation of catheter material (25).

Conclusion

Hydrophilic catheters were found to have a weaker NBCA-catheter bond strength than nonhydrophilic catheters. Also, hydrophilically coated catheters have a lower endovascular friction, allowing a greater proportion of any applied force at the catheter hub to be transmitted to the catheter tip. These properties should make hydrophically coated microcatheters less prone to permanent endovascular fixation during acrylic embolization.

Additionally, we found that different NBCA adhesives (Histoacryl and Avacryl) may have significantly different bonding characteristics with microcatheters. Use of the NBCA type with the least catheter adherence would also lessen the chance of endovascular catheter fixation.

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