Thrombogenicity of Teflon versus copolymer-coated guidewires: evaluation with scanning electron microscopy.

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Thrombogenicity of Teflon Versus Copolymer-Coated Guidewires: Evaluation with Scanning Electron Microscopy

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Utilizing the scanning electron microscope, we compared a new guidewire with copolymer coating with standard Teflon-coated, coiled-spring guidewires in both clinical and in vitro settings. Intense thrombogenicity was observed with the Teflon-coated guidewires with formed thrombi ranging in size from 50–100 μm. No formed thrombus was noted on any of the specimens of the copolymer guidewire, although isolated clumps of platelets and erythrocytes without fibrin strands were seen infrequently.

We conclude that the copolymer guidewire is markedly less thrombogenic than Teflon-coated guidewires.

Thrombogenicity of angiographic guidewires [1–8] and catheters [9–17] has been a concern of angiographers who use the Seldinger technique since the appearance of early reports describing cerebral embolism and postcatheterization femoral thrombosis. Recently, a new guidewire with a smooth copolymer coating has become available for routine clinical use [18, 19]. The copolymer coating is composed of 2-hydroethyl methacrylate, a hydrophilic monomer, and styrene, a hydrophobic monomer. Utilizing the scanning electron microscope (SEM) we examined this guidewire both in vivo and in vitro to determine its thrombogenicity and to compare it with the standard Teflon-coated, coiled-spring guidewires presently in use at our institution.

Materials and Methods

Clinically available guidewires* of 150 cm in length and 0.035 in. in diameter were utilized in both the in vivo and in vitro experiments. The in vivo guidewires were used clinically for femorocerebral angiography in conjunction with 5-French femorocerebral catheters and were prepared for SEM at the completion of an angiographic study (Figs. 1B, 2B, and 2D). The amount of time that the guidewire was within the patient was recorded. No patient received anticoagulants prior to or during the procedure, except for 4000 units of heparin within 1000 ml of normal saline, which was used for flushing the catheters. After each use, the guidewires were wiped with a gauze pad soaked in the heparinized flush solution.

An in vitro experiment was performed for the reason that significant clots may be stripped at the catheter tip upon withdrawal of a guidewire through the catheter. We decided not to use a large-bore catheter for the in vivo experiment in order to avoid the risk of femoral artery thrombosis.

The in vitro guidewires were placed in arterial blood, obtained from a patient undergoing angiography, for a variable period of time ranging from 90 to 360 sec. Prior to fixing, these guidewires were also wiped with the heparin-soaked gauze pad to simulate the clinical situation. (Figs. 1C, 1D, 2C, and 3). The Teflon- and copolymer-coated guidewires were treated similarly. Processing for SEM to preserve blood elements that may be adherent to the guidewires included fixation for at least 12 hr in cold 2% glutaraldehyde solution that was buffered with 0.1 mol/l sodium cacodylate. After they were given buffer rinses and dehydrated in graded ethanols, all specimens underwent critical-point drying with liquid CO_2 and were coated with gold-paladium prior to SEM. The fixation, dehydration, critical-point drying, and metal coating were done with standard, well-accepted techniques to preserve biological

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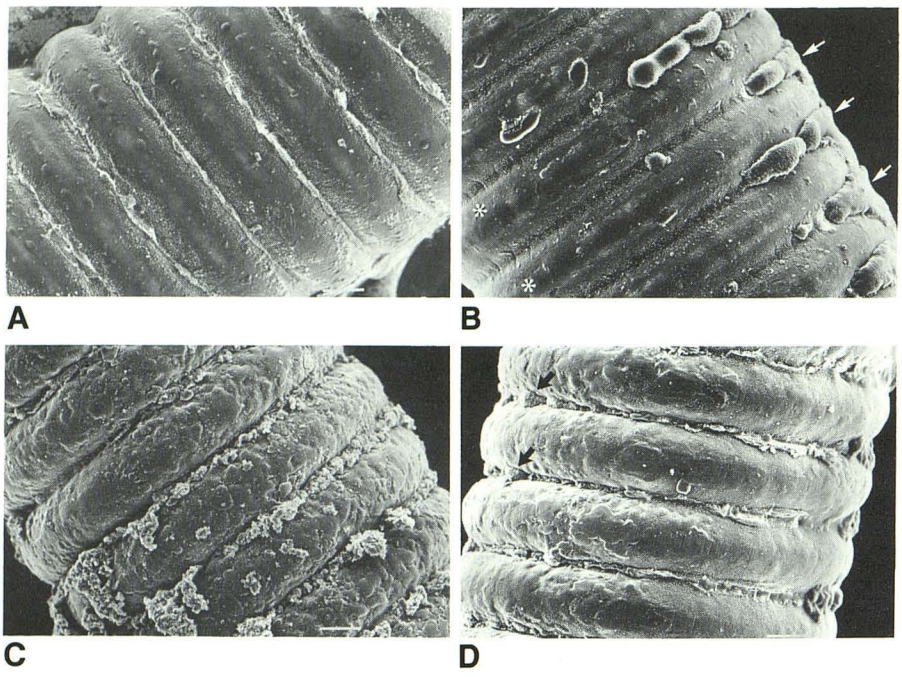

Fig. 1.—Scanning electron micrographs (SEMs) of Teflon-coated, coiled-spring guidewires.

***A*, SEM (×100) of a Teflon guidewire control demonstrates an irregular surface with flaking of Teflon coating noted within interstices of guidewire. Amorphous debris, probably representing flakes of Teflon coating, is seen on surface of guidewire.**

***B*, SEM (×100) of an in vivo Teflon guidewire used for 360 sec clearly demonstrates thrombi within interstices of coiled-spring guidewire and along lateral surface (*arrows*). The clots measure greater than 100 μm in length. During clinical use the guidewire had been wiped with a heparin-soaked gauze pad. Less than 30% of the surface had been wiped (*asterisks*).**

***C*, SEM (×100) of an in vitro Teflon guidewire that was in contact with human blood for 180 sec. Thrombus is clearly evident within interstices and protruding onto surface. Most of the thrombi are from 50 to 100 μm in length. Wiping with a heparin-soaked gauze pad did little to dislodge any thrombi from the interstices of this coiled-spring guidewire.**

***D*, SEM (×100) of an in vitro Teflon-coated guidewire in contact with human blood for only 90 sec. There are small thrombi (*arrows*) measuring up to 50 μm in the interstices. It is clear that heparinized gauze pad will not come in contact with this early nidus of thrombus during wiping.**

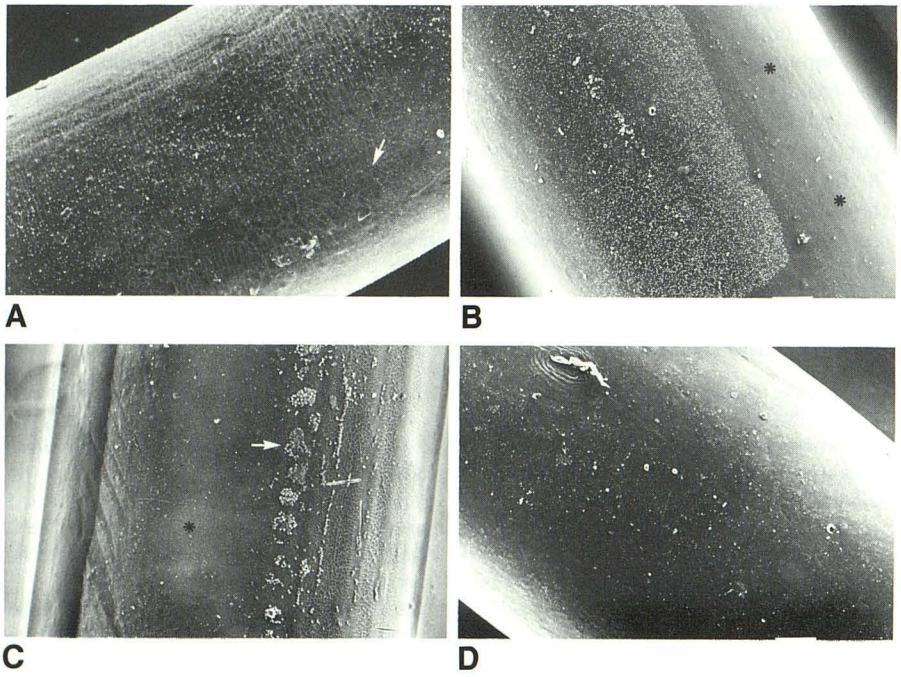

Fig. 2.—Scanning electron micrographs (SEMs) of copolymer guidewires.

***A*, SEM (×100) of an unused copolymer guidewire demonstrates a fine reticulated pattern of microfissures. Debris on surface of guidewire represents small flecks of plastic coating and dust particles. Small fissures (*arrow*) are also noted.**

***B*, SEM (×100) of an in vivo copolymer guidewire used clinically for 270 sec. There are isolated erythrocytes and platelets scattered along surface of guidewire. The region of guidewire that is without blood elements (*asterisks*) is the surface that had been clinically wiped with a heparin-soaked gauze pad.**

***C*, SEM (×100) of an in vitro copolymer guidewire placed in human blood for 270 sec. Clumping of erythrocytes is observed in center image (*arrow*). Area where there are no blood elements (*asterisk*) is the surface of the guidewire that has been wiped with a heparin-soaked gauze pad. Note fine reticulated pattern of protein deposition, which possibly affords a protective coating that prevents clot formation.**

***D*, SEM (×100) of an in vivo copolymer guidewire used clinically for 1200 sec. There are isolated erythrocytes and platelets on the surface of this guidewire. In the upper left-hand corner is a small defect in surface of guidewire that has collected some debris, probably a fiber from a gauze pad. No formed thrombus is seen.**

structures, particularly blood cells and platelets [20]. Random micrographs were made of nonoverlapping fields at ×100, ×500, ×1000, and ×5000 magnification.

Sixty-four guidewire specimens were obtained and 36 were studied by SEM. Limitation of SEM time prevented examination of the other 28 specimens. Thirty-six copolymer guidewire specimens were obtained and 20 were examined with SEM. There were 11 in vivo specimens, eight in vitro specimens, and one unused control. Twenty-eight specimens were of the Teflon-coated guidewires, and 16 were examined by SEM. Seven of these were in vitro guidewires, eight were in vivo guidewires, and one was a control. The size of the thrombi was recorded for each blood clot that was observed.

Results

SEM clearly visualized any blood elements on the surface or within the interstices of the guidewires. These blood elements included platelets and red blood cells, either isolated or in clumps, as well as formed thrombi, defined as aggrega-

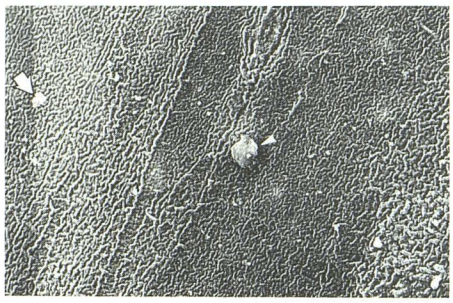

Fig. 3.—SEM (×1000) of an in vitro copolymer guidewire placed in human blood for 90 sec. A fine reticulated lacy pattern of protein deposition is seen on surface of guidewire. Protein deposition probably represents a combination of albumin, immunoglobulins, prothrombin, and fibrinogen. Isolated erythrocytes (*arrowhead*) and platelets (*arrow*) are attached to the protein.

tions of blood platelets with fibrin strands and trapped erythrocytes. No differences were found between the in vivo and in vitro guidewires.

The Teflon-coated guidewire control specimen (Fig. 1A) had an irregular surface with flakes of Teflon within the interstices. Small particles of Teflon debris and dust were also noted. The Teflon-coated guidewires demonstrated thrombus formation of greater than 100 μm upon the surface and within the interstices of the guidewire in six specimens (Fig. 1B), and thrombi between 50–100 μm in two specimens (Fig. 1C). Clumps of platelets and/or red blood cells were seen on three specimens, and four specimens demonstrated no blood elements. The thrombi seen on the Teflon guidewires were observed as early as 90 sec (Fig. 1D) and were also noted on guidewires that were used for 180, 270, and 360 sec. Thrombi of 100 μm were seen on six Teflon-coated guidewire specimens. Notably, a thrombus of this size was observed on an in vivo guidewire used for only 90 sec, and on in vivo guidewires used for 360 sec. Thrombi of 100 μm were observed on in vitro guidewires exposed to arterial blood for 180 and 270 sec.

The control copolymer guidewire specimen, which was not exposed to blood, showed a reticulated pattern of microfissures and isolated larger fissures, with debris, presumably flakes of copolymer, and dust particles (Fig. 2A). The surface of the guidewire was smooth (i.e., lacking interstices), since it had no coiled spring within it. The copolymer guidewire demonstrated isolated platelets or red blood cells in 17 specimens (Fig. 2B). In three specimens, clumps of platelets and/or red blood cells were observed but none was greater than 20 μm (Fig. 2C). No formed thrombus was demonstrated on any of the copolymer guidewires. One in vivo guidewire that was examined was used for a cumulative time of 1200 sec and failed to demonstrate any evidence of thrombus (Fig. 2D).

SEM at ×1000 and ×5000 magnification demonstrated an amorphous coating on both the Teflon and copolymer guidewires, presumably representing blood protein (Fig. 3). The pattern of protein coating on the copolymer guidewire had a reticulated lacy pattern that seemed to correspond to the reticulated pattern of the copolymer coating seen on the control guidewire (Fig. 2A). This pattern of protein deposition was not observed on any of the Teflon-coated guidewire specimens.

Discussion

Our results confirm the intense thrombogenicity of Teflon-coated, coiled-spring guidewires both in vitro and in vivo. Thrombi were noted on these Teflon guidewires that had as little as 90 sec of contact with arterial blood. The thrombi formed primarily within the interstices of the guidewire, and also on its surface. They are not affected by wiping with a heparin-soaked gauze pad. In fact, it was visually estimated by SEM that less than 30% of the surface of a guidewire is wiped clean by one pass of a heparinized gauze pad after each use in clinical practice (Figs. 1C, 1D, 2B, and 2C).

No formed thrombus was observed on any specimen of the copolymer guidewire. The smoothness of the surface, the lack of interstices, and the copolymer coating are in all likelihood the reasons for the hypothrombogenicity. Isolated platelets and erythrocytes were noted to routinely cover the surface of the copolymer guidewire. Only infrequently (three of 19 specimens) was any evidence of clumping noted. A copolymer specimen that was used for 1200 sec in one patient showed only isolated platelets and erythrocytes covering the guidewire. The inevitable conclusion from our study is that the copolymer guidewire is less thrombogenic than the currently used Teflon-coated, coiled-spring guidewires.

SEM at ×1000 and ×5000 magnification demonstrated a protein covering, which was much thicker on the copolymer guidewire, and presumably represented deposition of albumin, immunoglobulin G, prothrombin, and fibrinogen on the surface of the guidewire [19]. SEM demonstrated a fine reticulated pattern of protein deposition on the copolymer surface not seen with the Teflon-coated, coiled-spring guidewire. We believe that this protein covering of the copolymer guidewire affords a protective coating that prevents thrombus formation. This is in contrast to the speculations of Horbett and Weathersby [19], who suggested that this protein coat may be the precursor to clot formation. Our study does not support their contention, since the thick protein deposition occurred on the copolymer guidewire, which did not exhibit any thrombus formation. The reticulated pattern of protein deposition suggests that a specific protein binding pattern may be responsible for the hypothrombogenicity of the copolymer guidewire. The precise chemical or physical properties responsible for the adherence of protein to the surface of the copolymer guidewire were not elucidated by our study.

Although our study was not designed to evaluate the effect of wiping guidewires with heparin-soaked gauze pads after each use, which is our current routine during angiography, we visually observed with SEM that less than 30% of the guidewire is affected by this process. Debris, presumably from the gauze pad used for wiping, was seen to be attached to the Teflon-coated guidewire, whose irregular surface appeared to trap the fiber strands. Defects on the copolymer surface also seemed to trap fiber strands (Fig. 2D). We are in the process of examining a wipe that will affect the entire

surface of the guidewire. Other wiping materials, such as Tefka wires, were not evaluated.

A clinical comparison of the copolymer guidewire with the Teflon wire was not scientifically evaluated. Once we became accustomed to the hydrophilic (slippery) nature of the copolymer guidewire, which is its major disadvantage, we found that the angled, distal tip of the guidewire allowed easier catheterization of small vessels. The copolymer guidewire could be torqued into vessels much easier than could the Teflon-coated wires. Catheters followed the copolymer guidewire better than the Teflon wires, and the copolymer guidewire is virtually unable to be kinked.

We conclude that the copolymer guidewire when compared with the Teflon-coated, coiled-spring guidewire is markedly less thrombogenic as demonstrated by scanning electron microscopy. It does not initiate thrombus formation for up to 1200 sec in clinical use. Because of our results, the copolymer guidewire has become our standard guidewire in routine cerebral angiography. A reticulated protein coating of the copolymer guidewire is noted at high-magnification SEM, and this coating may act as a protective covering that prevents thrombus formation.

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REFERENCES

1. Anderson JH, Gianturco C, Wallace S, Dodd GD. A scanning electron microscope study of angiographic catheters and guide wires. *Radiology* **1974**;111:567–571
2. Durst S, Cramer R, Amplatz K. Flow cell evaluation of nonthrombogenic materials. *Radiology* **1973**;106:507–511
3. Formanek G, Frech RS, Amplatz K. Arterial thrombus formation during clinical percutaneous catheterization. *Circulation* **1970**;41:833–839
4. Frech RS, Cramer R, Amplatz K. A simple noninvasive technique to test nonthrombogenic surfaces. *AJR* **1971**;113:765–768
5. Haut G, Amplatz K. Complicated rates of transfemoral and transaortic catheterization. *Surgery* **1968**;63:594–596
6. McCarty RJ, Glasser SP. Thrombogenicity of guidewires. *Am J Cardiol* **1973**;32:943–946
7. Ovitt TW, Durst S, Moore R, Amplatz K. Guidewire thrombogenicity and its reduction. *Radiology* **1974**;111:43–46
8. Roberts GM, Roberts EE, Davies RL, Lawrie BW. Thrombogenicity of arterial catheters and guidewires. *Br J Radiol* **1977**;50:415–418
9. Amplatz K. A simple non-thrombogenic coating. *Invest Radiol* **1971**;6:280–288
10. Amplatz K. Catheter embolization. An editorial. *Radiology* **1968**;91:392–393
11. Anderson JH, Gianturco C, Wallace S, Dodd GD, DeJongh D. Anticoagulation techniques for angiography. *Radiology* **1974**;111:573–576
12. Cramer R, Frech RS, Amplatz K. A preliminary human study with a simple nonthrombogenic catheter. *Radiology* **1971**;100:421–422
13. Cramer R, Moore R, Amplatz K. Reduction of the surgical complication rate by the use of hypothrombogenic catheter coating. *Radiology* **1973**;109:585–588
14. Glancy JJ, Fishbone G, Heinz ER. Nonthrombogenic arterial catheters. *AJR* **1970**;108:716–723
15. Hawkins IF, Kelly MJ. Benzalkonium-heparin-coated angiographic catheters. *Radiology* **1973**;109:589–591
16. Kido DK, Paulin S, Alenghat JA, Waternaux C, Riley WD. Thrombogenicity of heparin- and nonheparin-coated catheters: clinical trial. *AJR* **1982**;139:957–961
17. Nekad MS, Klaper MA, Steggerda FR, Gianturco C. Clotting on the outer surfaces of vascular catheters. *Radiology* **1968**;91:248–250
18. Okano T, Nishiyama S, Shinohara I, et al. Effect of hydrophilic and hydrophobic microdomains on mode of interaction between block polymer and blood platelets. *J Biomed Mater Res* **1981**;15:393–402
19. Horbett TA, Weathersby PK. Absorption of proteins from plasma to a series of hydrophilic-hydrophobic copolymers. I. Analysis with the in situ radioiodination technique. *J Biomed Mater Res* **1981**;15:403–423
20. Robinson DG, Ehlers V, Hericen R, Herrmann B, Mayer F, Schurmann FW. *Methods of preparation for electron microscopy*. Berlin: Springer-Verlag, **1987**:23–44, 145–164