Large bore catheters with surface treatments versus untreated catheters for blood access

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ABSTRACT: Infection, thrombosis, and stenosis are among the most frequent complications associated with blood contacting catheters. Because these problems are usually related to surface properties of the base catheter material, surface treatment processes, such as ion implantation and ion beam assisted deposition (IBAD) (silver based coatings), can be used to mitigate such complications. Because these ion beam based processes affect only the near-surface region (approximately the outer 1 µm), there is little effect on bulk material properties. This study evaluated silver coated and implanted large bore catheters used for extracorporeal detoxification. In a 186 patient prospective study, 225 large bore catheters were inserted into the internal jugular or subclavian veins. 85 surface treated catheters (Spi-Argent, Spire Corporation, Bedford, MA-USA; n=39 acute catheters, n= 46 long-term catheters) and 28 catheters with surface treatment (Spi-Silicone, Spire Corporation, Bedford, MA-USA) were inserted in 90 patients. 112 untreated catheters placed in 96 patients served as controls (n = 62 acute catheters, n = 58 long-term catheters). After removal, the catheters were cultured for bacterial colonization using standard microbiologic assays. They also were examined using a scanning electron microscope (SEM). Bacterial colonization was observed in 8% of the treated catheters compared with 46.4% of untreated catheters. The SEM investigations showed all treated catheters to possess low thrombogenicity. Results of the study indicate that ion beam based processes can be used to improve thrombus and infection resistance of blood contacting catheters. (The Journal of Vascular Access 2001; 2: 97-105)

KEY WORDS: *Surface treated catheters, Spi-Argent, Spi-Silicone, Blood contacting catheters, Large bore catheters*

INTRODUCTION

In 1961 Shaldon et al. described for the first time the possibility of the percutaneously puncturing of the femoral artery and vein as a vascular access for hemodialysis treatment (1). In the following years this method was used only for the temporary access route for acute treatments to take care of all other peripheral vascular accesses for anastomosis. Kramer et al. presented in 1977 the percutaneous puncturing of the femoral artery for the spontaneous arterio-venous hemofiltration (2).
The catheterization of the femoral veins involves a lethal complication rate of 4% because Schwarzbeck et al. introduced in 1978 the catheterization of the vena cava superior, over the subclavian vein (3). But this method produces also more complications.
Despite all technical innovations in hemodialysis and apheresis treatments the problem of finding a temporary or permanent vascular access appears to have found no satisfactory solution. Temporary vascular access, in particular, still presents considerable problems and for this reason we introduced the cannulization of the superior vena cava over the internal jugular vein with a large bore catheter (4). Vascular catheters have become essential tools for management of hospitalized or chronically ill patients requiring intensive medical treatments such as extracorporeal detoxification procedures (5, 6). The increased use of such devices has been accompanied by a corresponding increase in complications, such as bloodstream infection and thrombosis (7). Infections are of particular concern because they can appear at any time, even years after implantation, and are not material-dependent. They are usually attributed to microbial colonization of

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the skin or handling of the catheters by the attending staff. Complication rates due to venous catheter related infection are reported to range from 34 to 40% (8, 9). Despite recent technical innovations in hemodialysis, problems related to temporary or permanent vascular access have found no satisfactory solutions. Temporary vascular access is particularly problematic.

In addition to infection, biocompatibility of synthetic materials is a major problem. The interaction of blood with a synthetic surface causes coagulation and activation of the complement system. Because of these problems, surface modification processes that can reduce the rate of infection or thrombogenicity, without adversely affecting basic catheter design and functionality, are of special interest. Ion beam assisted deposition (IBAD) coatings and implantation have been recently demonstrated to possess such characteristics.

This report describes a 4 year prospective clinical study in which 225 acute and long-term catheters were investigated. Eighty-five of the catheters were coated with silver using IBAD, and 28 implanted with ions, and the remaining 112 were without surface treatment. Catheters were examined for bacterial colonization and thrombus accumulation.

CATHETERS AND MATERIAL

The large bore catheter has been frequently modified over recent years and all models available are of a similar construction with single lumen (10). On the side of the catheter, depending on the model, 6-12 perforations are found, to garantee an effective blood flow and to prevent the catheter from adhering to the vascular wall. The conical tip allows for easier insertion of the catheter and prevents thrombus formation in the catheter while passing through to the blood stream.

In the last years various catheter models have become available such as single- double- and triple-lumen catheters for acute and chronic treatments (11-17). The techniques and insertions or implantations of the different vascular accesses are reported elsewhere and are not mentioned here (3-10).

The most of the available single- double- or tripple-lumen catheters have some deficiencies depending on the material. Not all catheters are radiopaque. No problem is experienced with polyurethane catheters after the incorporation of contrast media; however, the latter material may effect catheter durability when using Teflon. This was overcome by thicker catheter wall, but this caused endothelial irritation and early thrombus formation. Catheters providing radiocontrast are not absolutely necessary, however, because their position can be controlled more simply and gently with an intraatrial electrocardiogram lead (18, 19). The two most important criteria of any catheter material are a good tolerance and a low thrombogenicity (20, 21).

Another problem concerns the biocompatibility of the synthetic materials. Rarely do a material's properties perfectly match every requirement in a given application, and biomaterials are no exception. For instance, although a candidate orthopedic material may have ideal mechanical properties, it may elicit deleterious biological response, or a candidate biosensor with good electrical characteristics may corrode readily in the presence of body fluids (22).Therefore, it often becomes necessary to strike a comprise so that a material has acceptable properties in each pertinent area: This compromise is often made between bulk and surface properties. For example, in a product such as a hemodialysis catheter, which demands both good flexibility and low surface friction, the best candidate may be a slippery, less flexible material rather than a more supple one with unacceptably high friction.

Even after thorough consideration of all options and selection of the best available material, surface properties often continue to limit performance and function, in some cases prohibitively. Therefore the aim of the best function must be a minimal interaction with the surrounding biological system, and it was presented by Dathe (23):

1. Chemical	Biostabil, e.g. indifferent, do not get older or corrode
2. Physical	Observing the properties, elastic, good electrical characteristics
3. Morphologic	Smooth, slippery, water resistant, anti-adhesive
4. Physiologic	No disturbance of the fluid flow, laminary flow situation
5. Bacteriologic	Bacteristatic, bacterizide

The interaction of blood and synthetic surfaces causes activation of the coagulation and complement system. This lead to the adsorption of various proteins and the formation of a layer of protein on the synthetic surface. Thrombocytes and other blood cells adhere to this layer of protein so that thrombi may form. One solution is to employ surface engineering, the process of modifying surface properties while preserving bulk attributes. Surface engineering is now used to decisively and selectively improve the function and effective lifetime of the biomaterials used to manufacture catheters. A wide spectrum of biomaterial surface properties, including biological, mechanical, chemical, and other properties that directly influence biocompatibility and functionality, can be modified. Surface engineering is generally considered when a “good” surface is not good enough, when devices would not function without it, or when product differentiation is desired (22).

The importance of surface - engineered biomaterials has been recognized by major medical device companies, because surface modification processes can reduce the rate of infection, thrombogenicity, and other catheter-related complications without adversely affecting the basic design function of catheters.

Although the field is still essentially in is infancy, the range of services currently offered by surface treatment vendors is varied and continually expanding. Examples include conventional coating processes such as dipping and spraying; vacuum-deposition techniques (e.g. sputtering); and surface modification approaches such as diffusion (nitriding, carburizing), laser and plasma process, chemical platting, grafting or bonding, and bombardment with energetic particles (as in plasma immersion or ion implantation). Of the available techniques, those based on ionized particle bombardement have been particularly successful in biomaterial surface modification, primarily because they combine versatility and low-temperature processing with superior process control, reliability, and reproducibility (22).

In the following some new surface-treatment technologies that have been recently promoted as a means of improving catheter survival and performance are mentioned. Catheters whose surfaces were treated with silver or silicone (acute catheter n=67, long-term catheters n=46) were investigated after their removal in a Cam Scan scanning electron microscope. Bacterial colonization of the catheters was also investigated (24, 25).

Surface-treatment technologies for catheters

The ion beam-based technologies used for the treatment of catheters covered herein are ion implantation and ion beam-assisted deposition (IBAD). These processes are typically performed at low temperature under high vacuum. The affected layer in the ion implantation process, as well as the typical films deposited by the IBAD process, are on the order of 1 μm or less. Vacuum-compatible catheter materials may therefore be treated without adversely affecting bulk mechanical properties.

Both ion implantation and IBAD are of line-of-sight process, which implies that only the outer surfaces of the catheters can be treated directly however, parts with complicated geometries may be manipulated for uniform coverage of all surfaces. Two different methods of ion implantation were used: the ion implantation of silicone rubber catheters and the ion beam-assisted deposition of a silver coating (25). Silicone rubber is the material of choice for long-term indwelling catheters.

Ion implantation of silicone rubber has been proved to be a major break-through in removing its tacky surface, improving hydrophilicity, and significantly changing the ability of the surface to resist biodeposits in long-term indwelling medical devices. Suzuki et al. studied the reduction of thrombogenicity of silicone rubber as a result of ion implantation (26, 27). They reported that during the ion implantation process, hydrogen evaluation occurs.

Silver has been indicated as a good prospect for an infection-resistant coating material for catheters. The problem previously prevented the use of silver on catheters has been the inability to deposit adherent films of silver on flexible polymeric substrates. The IBAD process permits the formation of silver coatings at a relatively low temperature with extremely good adhesion that prevents delamination of the film during extended exposure to bodily fluids.

Spire Corporation (Bedford, MA, USA) has developed a silver-based film that can readily be applied to finished catheters. Spire referred to is proprietary patented technique for depositing the silver films as the Spi-Argent process (22, 28). The IBAD silver-deposited film has a low coefficient of friction, is highly uniform, and has demonstrated excellent adhesion.

Biocompatibility testing consisted of a cytotoxicity test and the USP Systemic Injection Test. Excellent results were obtained in both tests. In the cytotoxicity test (for both the coated and control silicone rubber samples), no evidence of intracellular granulation cellular swelling, or crenation was observed (28).

RESULTS

Commercially available catheters of silicone and polyurethane (Medizintechnik, Germany; Miramed, Italy, Medcomp, USA) which had an ion implantation of silicone (Spi-Silicone) or an ion beam-assisted deposition of a Silver coating (Spi-Argent) were used for insertion. In totally 113 surface treated acute or long-term large bore catheters in 90 patients were compared with 112 untreated

catheters in 96 patients over a 4 years period. The catheters were inserted in the internal jugular or subclavian vein (Tab. I).
Bacterial colonization of the catheter tip was observed in 8.0% in Spi-Argent in contrast to 46.4% in the untreated. There was no significant difference between the acute and long-term catheters in the same group. The surface treated catheter seems to be more infection resistant than the untreated catheter. The complication rates due to infections for untreated venous catheters are reported elsewhere and are between 8-40% (3, 8, 17, 30, 31).
The microbiological results of the 113 surface-treated and 112 untreated large bore catheters in 90 and in 96 patients respectively, are shown in Table II. The bacterial colonization was in the surface treated catheter significantly lower than in the untreated acute as well as in the long-term catheter.

TABLE I - SURFACE TREATED LARGE-BORE CATHETERS FOR BLOOD ACCESS

	Spi-Silicone			**Spi-Argent**			**Untreated**		
	(n)	**(n=pat)**	**mean *in situ***	**(n)**	**(n=pat)**	**mean *in situ***	**(n)**	**(n=pat)**	**mean *in situ***
Acute catheter	28	24	30.5 (1289)	39	33	25.9 (1-64)	62	46	24.7 (1-79)
Long-term catheter	-	-	-	46	33	173 (18-369)	50	50	134 (16-294)
Total	28	24	-	85	66		112	96	

TABLE II - MICROBIOLOGICAL RESULTS IN ACUTE AND LONG-TERM CATHETER (N=225) WITH (N=113), AND WITHOUT (N=112) SURFACE TREATMENT

	Surface treated acute catheter	**Surface treated long-term catheter**	**Total**	**Nontreated acute catheter**	**Nontreated long-term catheter**	**Total**
Catheter (n)	67	46	113	62	50	112
Skin (n)	28[1]	17[2]	45 (39.8 %)	39[1]	35[1]	74 (66.1 %)
Micro-Organism	20x S.epidermid. 4x S. aureus 4x pseudomonas	14x S. epidermid. 3x S. aureus		14x S. epidermid. 12x S. aureus	28x S. epidermid. 7x S. aureus	
Blood Culture (n)	5[3]	11[4]	16 (14.2 %)	36[3]	28[2]	64 (57.1 %)
Micro-Organism	3x S. epidermid. 2x S. aureus	4x S. epidermid. 7x S. aureus		6x S. epidermid. 2x Saprophyte 20x S. aureus	10x S. epidermid. 14x S. aureus	
Catheter tip (n)	4[5]	5[6]	9 (8.0 %)	30[5]	22[6]	52 (46.4 %)
Micro-Organism	3x S. epidermid. 1x S. aureus	3x S. epidermid. 2x S. aureus		4x S. epidermid. 1x Saprophyte 17x S. aureus	7x S. epidermid. 13x S. aureus	

[1] p = 0.1106, [2] p= 0.0077, [3] p= 0.0001, [4] p= 0.0441, [5] p= 0.0059, [6] p = 0.0166

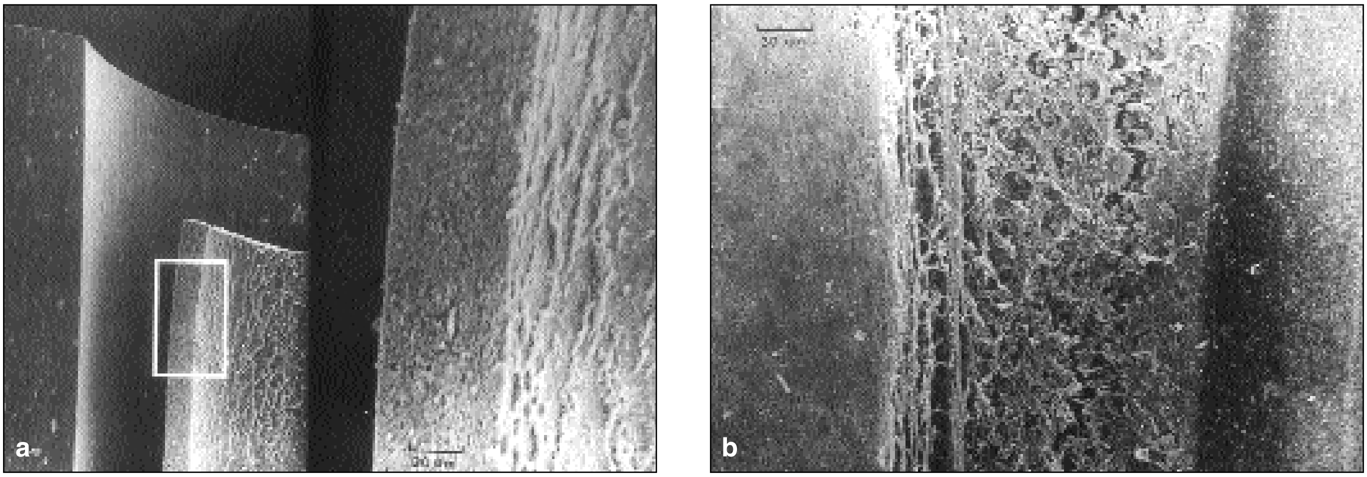

Fig. 1 - ***Thrombus completely covering the inner surface of a Teflon catheter. a) catheter after in-dwelling time of 54 days; b) magnification of the thrombus which shows the three layers.***

The most dangerous complications aside from accidental puncture of an artery are abscesses, or septicemia. The high infection rates do not depend on the route of vascular access (3, 9, 31). These catheter related complications are contributing factors to the increasing cost of medical care. They are responsible for patient readmissions and longer hospital stays as well as patients discomfort, morbidity, and occasional mortality. As such, new surgical techniques, catheter materials, and therapeutic drugs that influence performance and longevity of catheters are of great interest to the medical community (32, 33). Feldman et al. calculated in 1996 the costs of the morbidity due to catheter infections will soon exceed $1 billion per year (17). Therefore he demanded to reduce vascular access-related morbidity, that strategies must be developed not only to prevent and detect appropriately early synthetic vascular access dysfunction, but to better identify the patients in whom radial arteriovenous fistula is a viable clinical option.

Silver leaching was also evaluated by measuring the serum silver concentrations in 21 patients before insertion and after removal of the catheters. Silver concentrations were measured by the atomabsorption method. While the catheters were in the bloodstream, the serum silver level increased from 1.3 to 6.9 µg/dl (range 0.6-21.9 µg/dl) in acute catheters and from 3.4 to 19.6 µg/dl (range 0.5-44.2 µg/dl) in the long-term catheters. The serum silver level returned to normal several days after the catheters were removed. No toxic serum concentration of silver was observed in the investigated patients.

On the untreated catheters, layers of protein-containing erythrocytes, thrombocytes, and leukocytes, both on the inner and outer surfaces of the catheters, appeared after more than 3 days *in situ*, with the fibrin barely forming a lattice. However, large thrombi, completely filling the lumen and the lateral openings, were also observed. In addition, erythrocyte aggregates and agglutinated thrombocytes were also sometimes present. Thrombocyte adhesion possibly precedes erythrocyte agglutination.

After 8-10 days or more *in situ*, untreated catheters often were covered completely with a three layer deposit. The free surface of the thrombus consisted of dense longitudinal fibrin fibers. Underneath there was a loose fibrin structure in which numerous blood cells were embedded.

Another dense layer of proteins was located directly on the catheter surface. These thrombi were 3 to 90 µm thick, with the thickness depending on the time the catheter remained *in situ* (8).

Longer *in situ* times cause fibrin filaments to form on the edges of the thrombus. In the areas free of thrombi, numerous monocytes were found in different phases of adhesion, with ruffle formation (a structure normally developed by free cells only *in vitro*). Representative investigation with scanning electron microscope (SEM) of the untreated catheter is shown in Figure 1. The figure shows the inner surface of an untreated catheter which was completely covered with a second layer after *in situ* of 54 days.

In contrast to the results observed on the untreated catheter, catheters with the treated surfaces showed very low thrombogenicity and a low contamination rate. Catheters *in situ* for 1-2 weeks showed no deposits. Even after 2 months, no deposits of plasma proteins or blood cells could be seen by SEM. The outer surface is uneven and ridged, but without any

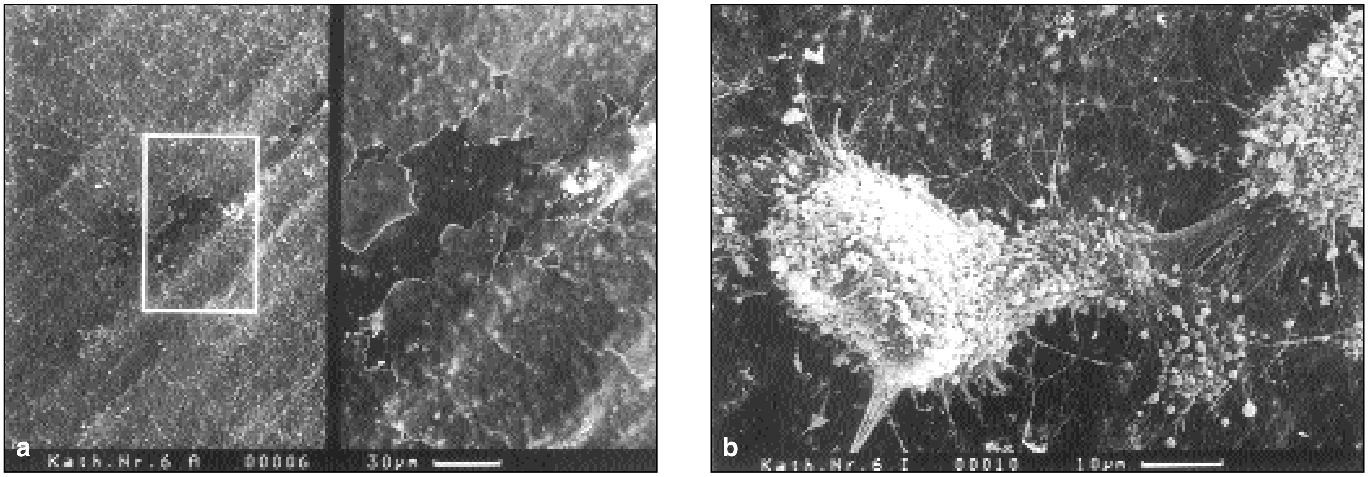

Fig. 2 - ***Surface treated catheter (Spi-Silicone) after* in situ *time of 38 days. a) outer surface of the Spi-Silicone catheter without any deposits; b) inner surface of the Spi-Silicone catheter with a thrombus formation.***

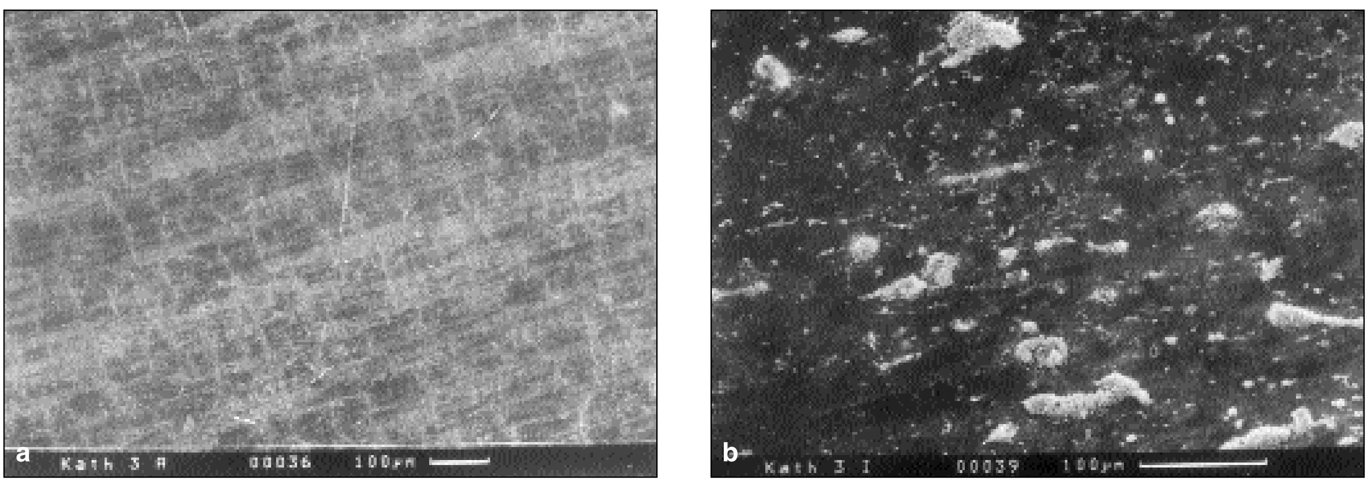

Fig. 3 - ***Surface treated long-term catheter (Spi-Argent) after* in situ *time of 68 days. a) outer surface of the Spi-Argent catheter without any biodeposits; b) inner surface of the Spi-Argent catheter with different biodeposits.***

deposits. By contrast, the inner untreated surface shows a thrombus with fibrin, erythrocytes, thrombocytes, and other blood components (Fig. 2). Figure 2 shows the inner and outer surface of a Spi-Silicone catheter which was removed after 64 days because a arteriovenous fistula became available.

The SEM investigations of surface treated long term catheters showed similar results. The outer surface showed no blood deposits. Even on the inner surface of these catheters, only small blood deposits with fibrin and erythrocytes were seen. Significantly fewer biodeposits were observed on the untreated inner surface of the Spi-Argent catheters than on the untreated catheters (Fig. 3). The figure 3 shows the outer and inner surface of a Spi-Argent long-term catheter after *in situ* time of 68 days. It seems that the silver ions on the outer surface may have an influence through the catheter wall, which increases with decreasing wall thickness.

DISCUSSION

Catheterization with large-bore catheters has replaced the previous use of a Scribner shunt, and is being increasingly used. Puncturing the internal jugular or the subclavian veins for temporary venous access is usually successful. The most dangerous complications, aside from accidental puncture of an artery, are abscesses or

TABLE III - POTENTIAL HEALTH CARE COST REDUCTIONS THAT COULD BE ACHIEVED THROUGH THE USE OF SURFACE TREATED CATHETERS

Device	Hemodialysis	Average infection (%)
Annual usage (devices)	125,971	
Infection rate (%)	5-20	Rate: 12
Cost ($) of complication (due to infection)	3,517	
Cost ($) of coating	12	
Reduction of infections (%)	10-65	Reduction 40
Market size (average/year) ($)	12.6 million	
Price ($) of each device (surface treated)	120	
Savings ($) per year by using surface treated devices	17.7 million	Reduction 40

septicemia. These catheter-related complications are contributing factors to increasing cost of medical care. They are responsible for patient readmissions and longer hospital stays as well as patient discomfort, morbidity, and occasional mortality. In addition to colonization biocompatibility of a catheter material is an important contributing factor to a successful clinical outcome, particularly in catheters that remain *in situ* for several weeks or months. Although it has improved with centrally placed catheters, the incidence of catheter clotting was previously very high.

The most dangerous complications, aside from accidental puncture of an artery, are abscesses or septicemia. Infection rates range from 5% to 30%; these rates do not depend on the route of vascular access (34-38, 40). As such, new surgical techniques, catheter materials, and therapeutic drugs that influence performance and longevity of catheters are of great interest to the medical community (40, 41).

To reduce infection rates and thrombogenicity, coated catheters and cuffs were investigated (42-47, 49-51). The clinical results of our investigated patients show a significantly reduced infection rate (14.2% vs 57.1%) in treated versus control catheters, a reduction of more than 75%. Silver ions are bacterizide, therefore no bacteria growth is possible on the catheter surface. The thrombogenicity also was lower and dependent on the *in situ* time. Generally, only small deposits were observed on the treated surfaces. With the silver surface treatment, a very smooth metallic surface was obtained which was responsible for a lower thrombogenicity rate. The activation of coagulation factors as the catheter surfaces was not investigated. Silver ions are bacterizide, therefore no bacteria growth is possible on the treated catheter surface. The clinical studies demonstrated the efficacy of the surface treated catheters.

Ion beam-based surface treatment technologies possess good reliability and reproducibility for treating catheters (33). Silver coated catheters can be used in blood-contacting applications up to oncology. In addition to reducing patient discomfort, significant savings in treatment costs can be realized using such processes, according to a calculation by Bambauer (32, 33, 47). For example, Table III shows representative health care cost savings for hemodialysis catheters, given specific infection rates and potential infection rate reductions achieved by treated catheters. The cost analysis was calculated by the literature and the available costs of different companies which distribute these catheters. The results showed that the surface treated processes for catheters can be used in blood contracting applications for all extracorporeal detoxification method.

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