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Design of a simulated urethra model for the quantitative assessment of urinary catheter lubricity

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Catheters designed for intermittent urological catheterization should possess appropriate lubricity and mechanical properties to ensure optimal clinical performance. However, the lack of a reproducible *in vitro* method that simulates clinical use makes it difficult to evaluate the lubricity of urinary catheters and other devices for urethral insertion. Therefore, this study describes a suitable method based on use of a Texture Analyzer to characterize the lubricity of such devices. The novel method was susequently applied to the evaluation of commercially-available intermittent urinary catheters. In addition, other important physicochemical properties of these catheters were examined, namely Young's modulus, degree of hydration and morphology. Catheter lubricity was quantified, using a Texture Analyzer, by measurement of the forces required for insertion and removal of the device from two model substrates, agar and mucin-coated silicone tubing. Significant differences in lubricity were identified between the commercially-available catheters, with Aquacath and Lofric exhibiting the lowest forces of insertion and removal. There were no significant differences between the extent of hydration between the catheters, with the exception of Uro-flo which exhibited the lowest hydration. Therefore, the differences in lubricity were not directly related to the extent of hydration. The forces required for insertion/removal of all catheters were markedly greater in the simulated mucin model than in the agar substrate and the former, simulated urethra model, was accepted to mimic more accurately, the *in vivo* situation. Significant differences were observed between the Young's Moduli of the catheter biomaterials, with Aquacath possessing the largest value. In conclusion, this study has described the use of a texture analyzer and polymeric substrates for the evaluation of biomaterial lubricity. Using these methods, Aquacath and Lofric catheters exhibited greatest lubricity. However, following additional consideration of the mechanical properties of these biomaterials, Aquacath possessed the most appropriate physicochemical properties for use in intermittent catheterization.

Introduction

Intermittent catheterization involves the passage of a single catheter into the bladder, via the urethra, to periodically drain urine from the bladder and to regain urinary continence [1]. Typically, it is indicated for patients who are either chronically incontinent or have intractable urinary retention, e.g. multiple sclerosis, spina bifida, or as a result of spinal injury [2]. As these patients often suffer from incontinence and are susceptible to urinary tract infections, intermittent catheterization can prevent or significantly reduce these problems [3]. For patients who will require intermittent catheterization for long periods of time, intermittent self-catheterization (ISC) is encouraged. These patients are advised to catheterize at least four times daily [4]. Typically, intermittent catheters are composed of a thin, hollow tube manufactured from a flexible but firm material, usually PVC, that is available in three lengths (adult male, adult female and child) and a range of sizes. Most patients use the Nelaton type catheter, i.e. a straight-tip catheter with a rounded end and one or two eyelets near the tip. The mechanical properties of these catheters are important determinants of clinical efficacy/acceptability and, characteristically, maximum ease and comfort of insertion may be generally achieved using a fairly rigid catheter with smooth shaft and eyelets [5].

The importance of preventing periurethral contamination coupled with the importance of surface lubricity of

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the catheter surface has long been recognized in catheter design [6]. For patients who have experienced difficulty inserting the catheters, excessive use of lubricating gel should be discouraged as this has been shown to allow contaminants to be transported to the bladder and may cause stinging and urethral irritation during catheterization [7]. To overcome this difficulty some catheters intended for intermittent use are coated with lubricious hydrophilic polymers [8]. When soaked in water for at least 30 s these coatings become slippery and so decrease the force and friction associated with urethral insertion [5]. In a pilot study, most patients preferred the hydrophilic-coated catheter to a regular PVC catheter with applied lubrication [9].

Despite the continuing commercial development of intermittent catheters by manufacturers, there is currently a lack of an appropriate *in vitro* model to simulate the acceptability of insertion of a range of commercially available catheters. Therefore, the initial aim of this investigation was to develop a reliable appropriate *in vitro* urethral model to characterize and compare the insertion and removal properties of commercially available intermittent catheters. Additionally, in light of the clinical importance of the mechanical properties of intermittent urinary biomaterials [5, 10], the tensile properties of commercially available intermittent catheters were also investigated. Therefore, this study represents the first comparative investigation of the lubricity and mechanical properties of commercially available intermittent urinary catheters and will thus be of assistance to clinicians in their selection of the most appropriate catheter, based on its physicochemical properties.

Materials and methods

Chemicals

Crude porcine gastric mucin was purchased from Sigma Chemicals Ltd., Poole, Dorset, U.K.

Silicone tubing (inner diameter 3.27 mm; outer diameter 4.77 mm) was employed in the examination of biomaterial lubricity and was purchased from Davidson and Hardy, Belfast, Northern Ireland.

Bacteriological agar was purchased from Oxoid, Basingstoke, Hampshire, England.

All other chemicals were purchased from Sigma Chemicals Ltd., Poole, Dorset, U.K. and were of AnalaR, or equivalent, quality.

Commercially-available intermittent catheters employed in the study

Six commercially available intermittent catheters (of the Nelaton type) were examined in this investigation, namely:

1. Aquacath coated urinary catheter (EMS Medical); male; 12ch; Lot 0897/04; Exp 08/2000
2. Conveen Easicath coated urinary catheter (Coloplast); 12ch; Lot 91450.11; Exp 07/2000
3. Lofric single use urinary catheter (Astra); 12ch; Ref 9012; Lot 1266; Exp 06/2000
4. Puricat coated urinary catheter (Maersk); 12ch; Ref 515-040-212; Lot 511481; Exp 11/2000
5. PVC nelaton catheter (Simpla); male; 12ch; Code 0369612; Lot 102357; Exp 03/2002
6. Uro-flo silky hydrophilic coated catheter (Simcare); male; 12ch; Ref USCC12M; Lot 97D14; Exp 04/2000

Catheter type 5 above was the only catheter tested which did not have a hydrophilic coating.

Examination of the time to hydration for each catheter

To examine the hydration of each catheter, samples (3 × 3 cm, sectioned lengthways) were weighed and immersed in tap water for 30 or 60 s. Following this, the sections were removed, all excess water displaced from their surface using filter paper and the mass of absorbed water quantified gravimetrically. All determinations were repeated, at least, in triplicate.

Examination of catheter lubricity

These tests were designed to simulate the clinical insertion of a catheter into the urethra, in which either agar or mucin-coated silicone tubing were employed to mimic the urethral environment. In the first (agar) method, samples (60 mm in length, containing the catheter tip) were hydrated in water for 30 s, as recommended by the manufacturers, and then clamped within the upper grip of the Stable Micro Systems Texture Analyzer (model TA-XT2). The sample was lowered at a constant rate (10 mm sec^{-1}) to a depth of 20 mm into bacteriological agar (1% w/v in deionized water) at 20 °C, which had been maintained for two days at 40 °C until required for testing (Fig. 1). The sample was held in this position for 120 s to mimic the indwelling time *in vivo* for urine drainage. This indwelling time had been calculated by allowing 600 mL of water (average bladder capacity) to drain through an intermittent catheter. The catheter was vertically removed from the agar, once more at a constant rate (10 mm sec^{-1}).

In the second (mucin) method, crude porcine gastric

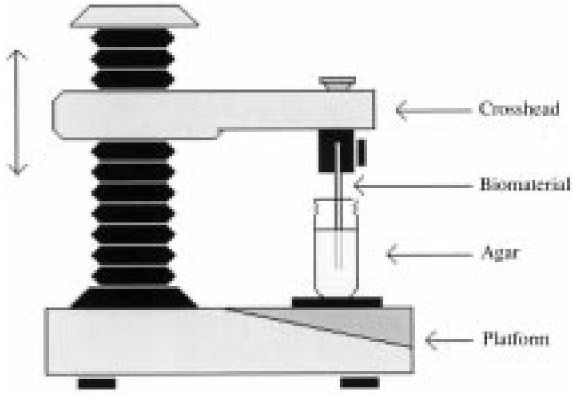


Figure 1 Diagrammatic representation of the texture analyzer as employed to quantify the force of insertion/removal of urinary catheters into/from agar.

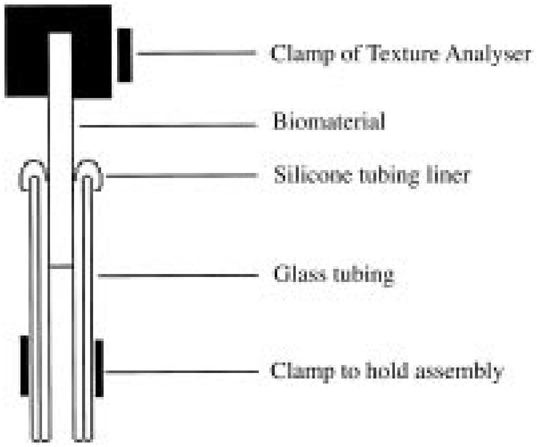


Figure 2 Diagrammatic representation of the simulated urethra model.

mucin (5% w/v) was dispersed in de-ionized water. A section of silicone tubing was inserted inside a glass pipette and the ends of this tubing carefully folded over the top of the glass tubing (Fig. 2). One end of the silicone tubing was blocked by the use of a seal, following which, the mucin dispersion was poured into the lumen of the silicone tubing and retained for a defined period (2.5 or 5 min). Prior to analysis, the seal was removed and the mucin dispersion allowed to drain. The silicone-lined glass pipette was clamped vertically between the lower grips of Texture Analyzer. Following hydration in deionized water for 30 s, the selected catheter was clamped between the upper grips of the Texture Analyzer. The tip of the catheter section was then lowered until initial contact was made with the leading edge of the silicone tubing. Each sample was then lowered to a depth of 20 mm into the vertically-clamped silicone tubing at a defined rate (10 mm $\sec^{-1}$). The catheter was held in this position for 120 s and then withdrawn from the tubing at a defined rate (10 mm $\sec^{-1}$).

From the resultant force–distance plot, the force required to both insert and remove the catheters from the either agar or the mucin-coated substrate were calculated.

Tensile analysis of commercially-available intermittent catheters

The tensile properties of the intermittent catheters under examination were investigated using a Lloyd JJ tensile tester (Lloyd Instruments, UK), as previously described [11]. Five samples from mid-sections of the catheters were cut into 50 ± 1 mm lengths and hydrated for 30 s, as previously described. These samples were then clamped between the grips of the tensile tester and the upper clamp elevated vertically at a constant rate (100 mm $\sec^{-1}$). The tensile tester was interfaced with a personal computer to allow remote control of the testing using the DAPMAT software. The Young's modulus of elasticity was calculated from the slope of the initial section of the stress-strain plot [11].

Microscopy of the intermittent catheters

The morphological properties of each catheter type (in the hydrated state) were examined using a dissection light microscope at a magnification of 16 ×.

Statistical analysis

The force required to insert and remove each catheter in the lubricity model, the extent of hydration following immersion in water and the Young's modulus of each of the commercially available intermittent catheters were statistically compared using a one-way analysis of variance. Furthermore, *post-hoc* comparisons of the means of the groups of observations were performed using Scheffe's test. In all cases, $p < 0.05$ denoted significance.

Results

The percentage increases in mass of each of the coated catheters following immersion in water for either 30 or 60 s are graphically displayed in Fig. 3. Following 30 s. hydration period, the extent of hydration of the Uro-flo catheter was significantly lower than any of the other catheters (Aquacath and Uro-flo $p = 0.0002$, Conveen and Uro-flo $p = 0.0004$, Lofric and Uro-flo $p < 0.0001$ and Puricat and Uro-flo $p = 0.0004$). Similarly, after 60 s. hydration, the Uro-flo catheter was shown to hydrate significantly less than Aquacath ($p = 0.0066$), Lofric ($p = 0.0025$) or Puricat ($p = 0.0101$). There were no significant differences in the extent of hydration of the other catheters under examination. In general, there were no significant differences observed between the extent of hydration of the catheters following 30 and 60 s. periods of immersion. However, exceptionally, the percentage increase in mass following hydration of Conveen for 60 s. was significantly lower than that following 30 s. immersion in water, indicating shedding of the polymeric coating.

Light microscopy was used to examine the effects of hydration on the surfaces of each catheter. Figs 4a and b illustrate the surface of the Lofric catheter, at 16 × magnification, non-hydrated and after 30 s hydration, respectively. The surface may be observed to lose its cracked appearance and became visibly smoother after hydration. A similar phenomenon may be observed for Aquacath (Figs 4c and d), Conveen (4e and f) and Puricat (Figs 4g and h).

The forces required to insert each catheter into and withdraw each catheter from an agar substrate are presented in Table I. The greatest force of insertion

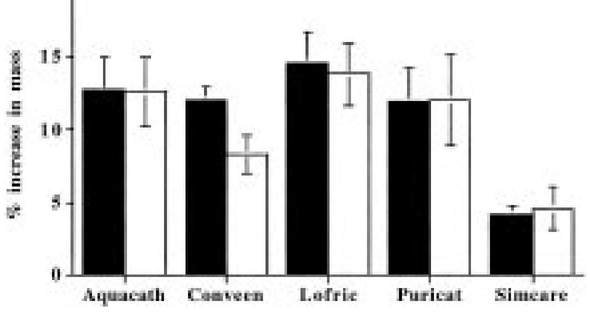


Figure 3 Percentage increase in mass of intermittent catheters following 30 and 60 s hydration in distilled water. Values shown are the mean and standard deviation of at least three replicates.

TABLE I Force required to insert and withdraw intermittent catheters from an agar substrate

Catheter	Force (N) required to insert	Force (N) required to withdraw
Aquacath (EMS Medical)	0.34 ± 0.02	0.09 ± 0.02
Conveen (Coloplast)	0.36 ± 0.01	0.16 ± 0.03
Lofric (Astra)	0.35 ± 0.02	0.07 ± 0.02
Puricat (Maersk)	0.36 ± 0.01	0.10 ± 0.01
PVC (Simpla)	0.42 ± 0.01	0.11 ± 0.04
Uro-flo (Uro-flo)	0.39 ± 0.02	0.19 ± 005

was displayed by the uncoated PVC (Simpla) catheter whereas the lowest insertion forces were associated with Aquacath and Lofric catheters. The forces required to insert the coated catheters into the agar were significantly less than those required to insert the uncoated PVC (Simpla) catheter (Aquacath and Simpla $p < 0.0001$, Conveen and Simpla $p = 0.0003$, Lofric and Simpla $p < 0.0001$, Puricat and Simpla $p = 0.0001$ and Uro-flo and Simpla $p = 0.0229$). However, there were no significant differences in the forces required to insert either Aquacath, Conveen, Lofric or Puricath ($p > 0.05$). Conversely, Lofric required the lowest force to withdraw from the agar, whereas Uro-flo required the greatest force. Indeed, Uro-flo required a significantly greater force to remove it from the agar than did Aquacath ($p = 0.0005$), Lofric ($p < 0.0001$), Puricat ($p = 0.0009$) or PVC ($p = 0.0032$). In addition, Conveen was also relatively difficult to remove from the agar requiring a greater force than Aquacath ($p = 0.0084$), Lofric ($p = 0.0011$), Puricat ($p = 0.0144$) or Simpla ($p = 0.0488$).

Fig. 5 graphically displays the force required to insert the catheters into the mucin-lined silicone tubing. No data concerning the force required for insertion of PVC (Simpla) catheters into silicone tubing, devoid of the mucin layer, has been quoted due to flexure of the catheter sample during the insertion process. The force required to insert the PVC (Simpla) catheter into the simulated (mucin-coated) urethra was significantly greater than those for the corresponding sections of Aquacath, Lofric or Conveen, at each concentration and dwell time of mucin ($p < 0.0001$). The forces required to insert sections of both Aquacath and Lofric were statistically similar and, furthermore, were significantly lower than for Conveen. Interestingly, neither the mucin concentration (2.5 or 5.0%) employed to coat the silicone tubing in the urethral model or the time of treatment of treament (1 or 5 min.) were observed to affect the force of insertion of the coated catheters ($p > 0.05$).

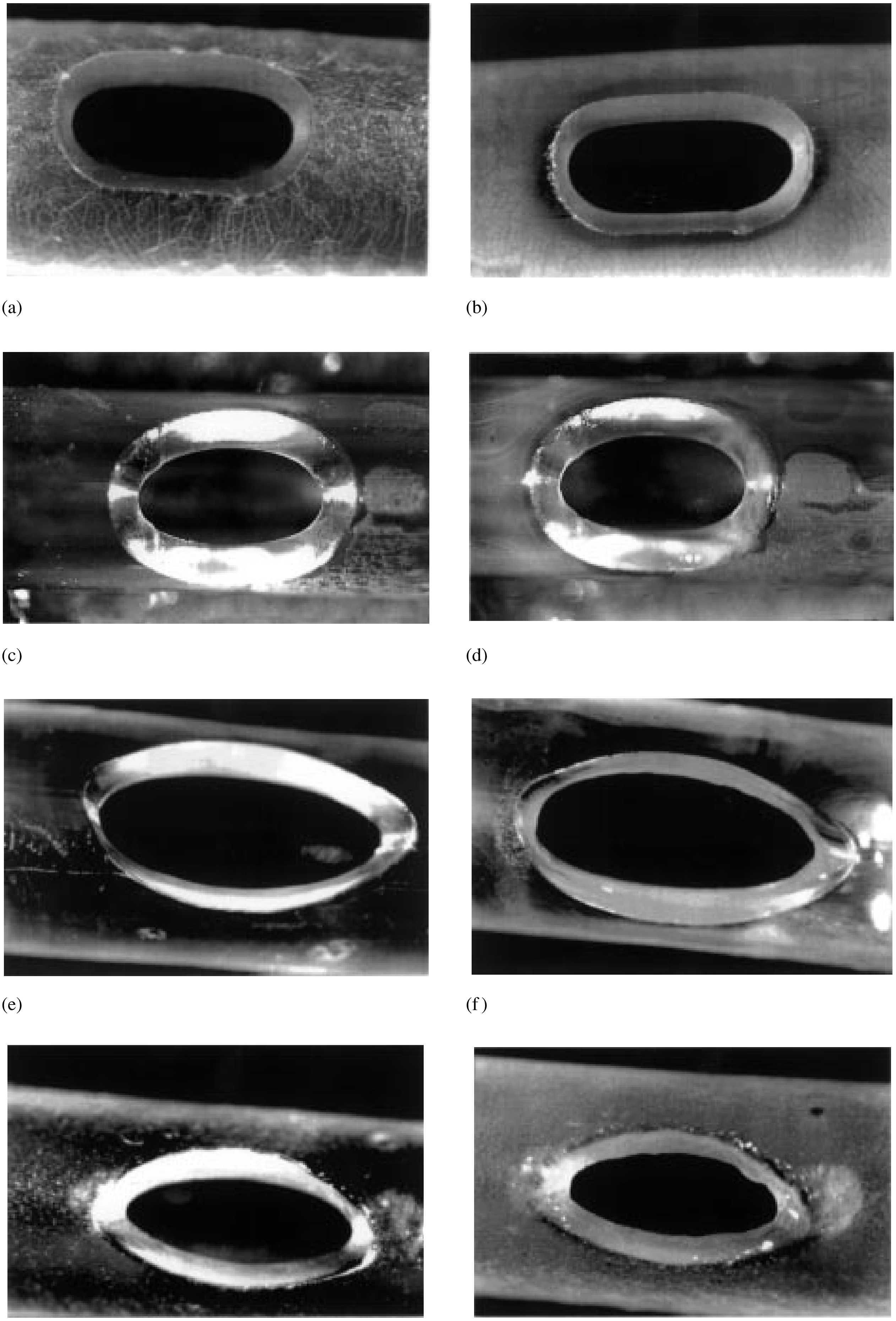
Fig. 6 illustrates the forces required to withdraw the catheters from the mucin-coated silicone tubing urethral model. Once more, the data concerning the insertion of the PVC catheter into non-mucin coated silicone tubing have been omitted. The force required to withdraw the PVC (Simpla) sections from the simulated urethra were significantly greater than those for the corresponding sections of Aquacath, Lofric or Conveen at each concentration and dwell time of mucin ($p < 0.0001$). The forces required to withdraw either Aquacath or Lofric from the simulated urethra were once more statistically similar and, additionally, significantly lower than for Conveen. Once more, neither the concentration of mucin coating nor the time of coating of the silicone tubing with mucin significantly affected the force required to withdraw the coated catheters from the urethral model.

The Young's modulus of each catheter under examination is graphically presented in Fig. 7. The highest and lowest Young's Modulus values were displayed by Aquacath and Puricat, respectively. Furthermore, the Young's Modulus of each catheter was significantly different from one another with the exception of Conveen and Lofric, which were statistically similar

Discussion

Catheters designed for intermittent urinary drainage should be easily inserted into the urethra following the recommended period of hydration. Two important physicochemical properties that influence the ease of insertion are the Young's modulus (rigidity) and lubricity. However, whilst the rigidity of biomaterials may be readily evaluated using tensile methods [11], there are no reliable methods to evaluate the lubricity of urinary catheters that provide information relevant to their clinical useage. This study has, therefore, corrected this deficiency by describing a method that simulates insertion of a catheter into the urethra, reflecting the resistance of the urethra to the insertion process.

For the most part, the catheters under examination in this study were coated with a hydrophilic polymeric material, which, following hydration, bestowed enhanced lubricity to the catheters. Therefore, prior to both the development of a reliable method to evaluate lubricity and, additionally, the use of this method to compare the lubricity of intermittent catheters, it was necessary to examine the rate of hydration of the catheters. Interestingly, whilst all catheters were observed to maximally hydrate after 30 s in water, the manufacturers' recommended period of hydration prior to insertion, differences were identified between the extents of hydration of some of these systems. In particular, the extent of hydration of Uro-flo was significantly lower than all others examined, most likely due to the polymeric nature of this coating. Furthermore, the overtly gelatinous nature of the coating on the Conveen catheter following hydration for 60 s. in distilled water may have accounted for the observed shedding in hydration studies. The effects of hydration on catheter morphology may be observed by light microscopy. All catheter surfaces were visibly smoother



(a)

(b)

(c)

(d)

(e)

(f)

(g)

(h)

Figure 4 Photomicrographs (16 ×) of commercially available intermittent catheters. Non-hydrated and hydrated Lofric (Figs 4a and b, respectively), non-hydrated and hydrated Aquacath (Figs 4c and d, respectively), non-hydrated and hydrated Conveen (Figs 4e and f, respectively) and non-hydrated and hydrated Puricat (Figs 4g and h, respectively). The period of hydration was 30 s.

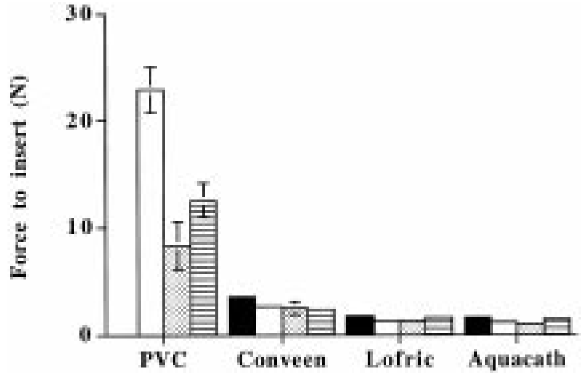


Figure 5 Effect of concentration of mucin dispersion and time allowed for coating of the silicone tubing on the resultant rorce required to insert intermittent catheters in the simulated urethral model. Key: ■ no mucin, □ 2.5% w/v mucin for 5 min, 5% w/v mucin for 1 min, 5% w/v mucin for 5 min. Values shown are the mean and standard deviation of at least three replicates.

in the hydrated state, thus allowing for more comfortable insertion, and hence greater comfort in use [5]. A previous study has also reported that a hydrogel coating effectively smoothed any surface irregularities of the underlying material, with hydration causing further smoothing [12].

The lubricity of all catheters was initially examined using agar to simulate insertion into the moist environment of the urethra. The choice of agar in this respect was based upon a previous study [13] in which agar was employed as the model matrix for the evaluation of biomaterial lubricity. In this, the authors described the time required to remove urinary biomaterials following application of a weight, applied at 90° to the agar matrix. In the current study, a texture analyzer was employed to provide the tensile stress and this offered several advantages over the previous method. Firstly, the accuracy and reproducibility of the measurement of lubricity were markedly improved and, secondly, the texture analyzer quantified both the force to insert and remove the urinary biomaterials from the chosen matrix.

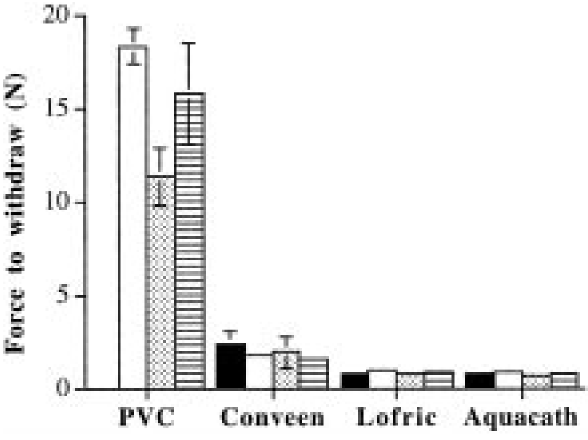


Figure 6 Effect of concentration of mucin dispersion and time allowed for coating of the silicone tubing on the resultant rorce required to withdraw intermittent catheters in the mucin-coated urethral model. Key: ■ no mucin, □ 2.5% w/v mucin for 5 min, 5% w/v mucin for 1 min, 5% w/v mucin for 5 min. Values shown are the mean and standard deviation of at least three replicates.

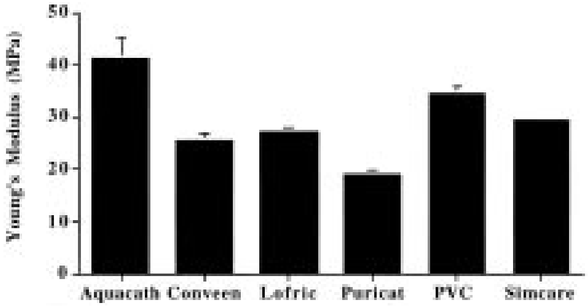


Figure 7 Young's modulus of commercially available intermittent catheters. Values shown are the mean and standard deviation of at least three replicates.

Using the texture analyzer and an agar substrate, significant differences were apparent between the force required to insert PVC (Simpla) and the coated catheters, with PVC being the most difficult to insert (Table I). However, following coating with agar, PVC was relatively easy to withdraw (Table I). Of all the hydrophilic-coated catheters, Uro-flo was the most difficult to insert into the agar. This may imply that the degree of hydration of the coating has some gross influence on the ease of insertion, as Uro-flo was found to imbibe least water on hydration (Fig. 3). Conveen and Uro-flo were more difficult to withdraw from the agar than the other coated catheters, possibly due to some interaction with the agar, however both Lofric and Aquacath catheters were relatively easy to insert and withdraw from the agar. These results show the benefits of the specific lubricious coatings for the reduction of possible urethral friction during insertion and withdrawal, so reducing possible urethral trauma.

Despite the advantages of the above method, further improvements were required to mimic insertion of a catheter into the urethra. In this regard, silicone tubing was employed as a simulated urethra as this offers resistance to catheter insertion, an important clinical consideration. Furthermore, as it has been reported that biomaterials may exhibit a range of frictional profiles *in vivo* due to various interactions with proteins, mucopolysaccharides and cells in the body [14], the inclusion of mucin (up to 5% w/v in deionized water) as a coating of the simulated urethra confered the additional benefit of simulating any catheter-bodily fluid interaction [15]. Therefore, this improved method quantified both the forces of insertion and removal of urinary catheters in a model that coupled both the inherent lubricity of the urethra (offered by the presence of mucin) and the natural resistance to catheter insertion and removal derived from the resistance of the urethral wall. Four representative catheters were then chosen for analysis in the simulated urethral model, PVC (standard), Conveen (intermediate difficultly to insert/withdraw from agar) and Aquacath and Lofric (highly lubricious nature). This test method identified greater differences between catheter performances than the previous (agar) test, as the resistance to insertion and withdrawal into the simulated urethra was much higher than into agar. This reflected the resistance to insertion and removal offered by the urethra, and consequently, these results are more representative of the clinical scenario. Insertion of the

PVC catheter into the tubing in the absence of mucin, was impossible due to high frictional resistance. The decreased force required to insert the coated catheters compared to PVC (Fig. 5) was highly significant, exhibiting the benefits of hydrophilic coatings for this purpose. Conveen required a greater force to insert into and withdraw from the simulated urethra than Lofric (or indeed Aquacath), thus agreeing with the findings of Waller *et al.* [16] who associated a significantly lower friction force (measured by a dynamometer) with Lofric than Conveen. Interestingly, in the case of the coated catheters, neither different dwell times or mucin concentration significantly affected the force required to insert/remove these systems in the simulated urethral model. This reflected the robust nature of the experimental method.

As previously described, the mechanical properties, especially rigidity, directly affect the ease of insertion/removal of urinary catheters in the clinical situation. In this regard, more rigid catheters have been reported to be easier to insert than their less rigid counterparts [1, 5]. In the current study, Aquacath was found to be the most rigid of the materials tested and, conversely, Puricat the most flexible. The uncoated PVC catheter was also less flexible than the coated catheters, with the exception of Aquacath. Aquacath, the most rigid of the catheters tested, was also easiest to insert into the agar. This result verifies the situation *in vivo* where patients have reported easiest insertion with more rigid materials [5]. This study has, therefore, highlighted the particular beneficial mechanical properties of Aquacath for intermittent catheterization.

In conclusion, this study has described the use of a texture analyzer, in conjunction with an appropriate substrate, either agar or mucin-coated silicone tubing to accurately and reproducibly quantify the lubricity of urinary catheters. Due to the resistance offered by the silicone tubing to the insertion/removal of the catheter biomaterials and, additionally, the inclusion of mucin, to simulate the natural lubricity of the urethra, it is proposed that, of the two substrates described, the mucin-coated silicone tubing more accurately simulates urethral conditions *in vivo*. For these reasons, this method is preferred for the *in vitro* assessment of urinary catheter lubricity. These methods were employed to examine any differences, between commercially available catheters, which could affect their performance and ease of use. Coated catheters were all found to be significantly easier to insert into agar than the uncoated PVC catheter, highlighting the usefulness for polymeric hydrogel coatings on such catheters. Of the coated catheters, Aquacath and Lofric exhibited the lowest forces of insertion and removal. As catheter rigidity is an important determinant of ease of insertion and removal *in vivo*, this property was examined using tensile analysis. Of all the catheters examined, Aquacath was found to possess the most appropriate properties of catheter rigidity and lubricity and thus should optimally meet the clinical demands of intermittent urine drainage.

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