BUDAPEST UNIVERSITY OF TECHNOLOGY AND ECONOMICS

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Summary of PhD dissertation

MEASUREMENT METHODS FOR THE DETERMINATION OF VISIBILITY AND MATERIAL PROPERTIES OF ANGIOPLASTY DEVICES

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Angioplasty is a commonly used minimal invasive procedure. The basic angioplasty devices are guidewire and intravascular catheters (guide and balloon) [1] [2] [3] [4]. The success rate of the angioplasty is 95% [5] [6] [7] [8] [9]. Flexibility and kinking resistance are two features of the basic angioplasty devices that play an important role in improving its success rates [10].

There are four requirements, which are characteristic not device specific to the guidewires, guide catheters and balloon catheters according to the current standards (biocompatibility, surface, corrosion resistance and visibility) [11] [12] [13].

Tests and measurement methods are recommended for determination and measurement of biocompatibility, surface and corrosion resistance. These standards have different recommendations for visibility measurement methods [11] [12] [13] and therefore, the manufacturer can test it using different methods. The current standard for the basic angioplasty devices does not contain objective measurement methods for determination, quantification of flexibility and kinking resistance. However, some standards, the U.S. Food and Drug Administration (FDA) and some articles describe different measurement methods for the above mentioned. The manufacturer can test it using different methods. As a result, the tested devices do not become comparable.

The long-term plan of this study was the comparison of the available guidewires, guide catheters and balloon catheters according to their visibility, flexibility and kinking resistance. The values described in the literature can be measured using different measurement methods and therefore, a method should be established which is suitable to measure these properties. It should:

- Be suitable for investigation of all available basic angioplasty devices.
- Quantify the visibility or the flexibility or the kinking resistance.
- Be quick and easy to perform.
- Provide data with repeatability and reproducibility.

Since all the medical devices are difficult to access, in this PhD dissertation, the aim was to develop, determine and test the measurement methods and not testing of all the available guidewires, guide catheters and balloon catheters. In case of the developing of the measurement method the first aim was the comparability therefore now these methods is not the very accurate measurement method.

Research objectives

1. To develop a measurement method for the objective determination of the visibility (verified the repeatability and reproducibility) based on the ASTM F640-12 standard, the U.S. Food and Drug Administration and based on earlier studies performed at the BME ATT Medical Research Group; which is suitable for quantifying, classifying, and comparing the guidewires, guide catheters and balloon catheters separately based on this property.
2. To develop a measurement method for the objective determination of the guidewires' flexibility based on the standards for bend tests, the U.S. Food and Drug Administration Guidance and based on earlier studies performed at the BME ATT Medical Research Group.
3. Implementation, testing and possible modification of the guide catheter flexibility measurement method according to standards for bend tests and the U.S. Food and Drug Administration, and the studying of the guide catheter behavior during the bending.

   To determine the change in flexibility along the guide catheter, as a function of the distance from the distal tip and the initial diameter.
4. Implementation, testing and possible modification of the guidewires' kinking resistance measurement method according to the literature (Schröder J.'s method), and the studying of the guidewire behavior during the kinking.

   To determine the change in kinking resistance along the guidewire by a method developed during those research, as a function of the distance from the distal tip.
5. To develop a measurement method which is suitable for objective quantification of the guide catheter's kinking resistance.

   To determine the change in kinking resistance along the guide catheter as a function of the distance from the distal tip and the initial diameter.

Results

Visibility measurement method

Based on earlier research performed in BME ATT Med., a method was developed to quantify the visibility of stents. This method was applied to guidewires, guide catheters and balloon catheters.

The main steps of the visibility measurement were the following:

1) Creating X-ray microscopic images of the investigated part of the medical device using parameters used during clinical practise.

2) Cutting out a specified length of the device part from the image and similarly cutting out a section of the background (here, the sample holder of the X-ray micoscopic system) of the same length as the device image section and converting it into greyscale, bitmap images.

3) Determining its visibility (in %) against the background using the image analysis software written at BME ATT Med.

It was determined that:

- In case of guidewire
  - The radiopaque tip of the guidewire should be investigated (if this part was not indicated by the manufacturer, then from the distal end).
  - The average visibility of two shorter parts (minimum 2.0 mm) illustrated the visibility of the guidewire.
  - To conduct these measurements, a curvature-free section was necessary. The two short sections investigated in this study did not contain curvature, neither for straight guidewire nor pre-shaped guidewire.
- In case of guide catheters
  - The marker or the X-ray absorbing material on the guide catheter should be investigated (if there were any).
  - If the catheter does not contain marker or the X-ray absorbing material, the first part of the catheter should be investigated (from the atraumatic tip to the first curve of the shape).
  - The first 10 mm of distal end should be investigated in case of the total guide catheters.

- The average visibility of two shorter parts (minimum 2.0 mm) could be used to characterise the visibility of the guide catheters.
- To perform visibility measurements, a curvature-free section was necessary. Therefore, the two investigated short sections selected did not contain curvature.

- In case of balloon catheters
  - The balloon markers should be investigated.
  - The average visibility of the markers characterised the visibility of the balloon catheters.
- The visibility of each medical device used in this study was compared to similar backgrounds (here, the sample holder of the X-ray microscopic system) using the self-developed measurement methods. Taking this into account, it was made sure to use equal background and image settings.

Flexibility measurement method

In case of objective determination of guidewire's flexibility, the FDA Guidance and method of Schröder J. was applied for the easy and practical implementation. For this measurement, a self-developed fixture was used. The main steps of the guidewire's flexibility measurement were the followings:

1) Gripping the guidewire in at the desired grip point at the lower grip of the tensile-testing machine.
2) Gripping a drilling rode with 0.5 mm radius into the upper grip.
3) Adjusting the distance between load and fixed end.
4) Placing the drilling rode with 0.5 mm radius above the load point.
5) Bending of the guidewire at the rate of 10 mm/min.
6) Recording the force which causes 45^{o} deflection angle while bending the guidewire.
7) Choosing three point force-displacement points from the force-displacement curve's rising linear part. The three points were at 30%, 60% and 90% of the maximum value of the force-displacement curve's rising linear part.
8) Determining the nominal bending stiffness from the force-displacement points ($\mathrm{NBS} = \frac{\mathrm{FL}^3}{3\mathrm{f}} + \frac{\mathrm{Fl}^2}{2\mathrm{f}}(\mathrm{L} - \mathrm{l})[\mathrm{Nmm}^2]$).
9) Determining the average nominal bending stiffness from the three force-displacement points for the given grip point, which characterises the flexibility of the given bending point with the given construction.

It was determined that the 10 mm grip point with centre load was suitable to determine the forces that causes 45° deflection angle and it was preferable to measure the

nominal bending stiffness. The nominal bending stiffness characterises the flexibility of the given bending point with given construction.

In case of objective determination of guide catheter's flexibility, the FDA Guidance and the recommendation from literature sources were applied but the bending point was not determined therefore, ten bending points were measured.

The main steps of the guide catheter's flexibility measurement were the following:

1) Measuring the outer diameter and deflection angle of the guide catheter at the bending point.
2) Placing the bending point marked on the catheter onto the gauge.
3) Bending the catheter around the gauge with the biggest radius.
4) Holding it in the same state for 5 seconds and then releasing it.
5) Measuring the dimension change perpendicular to the axis of bending and its deflection angle.
6) The bending was carried out for all gauges (from the biggest to the smallest radius) and the dimension change perpendicular to the axis of bending and the deflection angle after the bending was measured at all bending points on the catheter.

Using these measurement values and its statistical analysis, it has been defined that

- There was no distinguished location along the catheter, where deflection angle and dimension change perpendicular to the axis of bending was more likely to happen.

It was determined that

- Flexibility was the critical bending radius which was shown by the inflection point of dimension change perpendicular to the axis of bending's curve.
- It should be measured at two curvature-free parts taken from 100-200 mm and 200-300 mm sections from the distal end with minimum 20 mm distance between the bending points.
- Average flexibility of the two points characterised the flexibility of the guide catheters.

Kinking resistance measurement method

I have improved equipment to objective determination of guidewire's and guide catheter's kinking resistance. The measurement based on Schröder's work; he has a publication to measure kinking resistance of guidewires. The main steps of kinking resistance measurement are the followings (in case of guidewire and guide catheter too):

1) Insertion of the device into the fixed grip.
2) Gripping of the kinking point.
3) Measuring of deflection angle and in case of guide catheter the dimension change perpendicular to axis of bending. In case of measuring of the deflection angle only the deflection angle of the first 3 mm from the kinking point is measured. This deflection

angle is relevant; it is not affected by gravitation and the weight of the movable part of the device.

4) Fixation of the movable part of the device into the movable grip.
5) Kinking 5^{o} and keeping 5 seconds in this position.
6) Measuring the dimension change perpendicular to axis of bending during the kinking.
7) Releasing of the device's moving part.
8) Measuring of deflection angle (see 3^{rd} step).
9) Fixation of the movable part of the device into the movable grip.
10) Kinking 10^{o} and keeping 5 seconds in this position.
11) The measured kink angles are from 0^{o} to 120^{o} in case of guidewires and from 0^{o} to 130^{o} in case of guide catheters by 5^{o} steps. In case of guide catheter the dimension change perpendicular to axis of bending shall measure during the kinking, and in case of guide catheter and guidewire the deflection angle shall measure after the kinking.

It was determined that:

- In case of guidewires
  - The kinking resistance of both the shaft and the distal end was the critical kink angle that was shown by the inflection point of its respective deflection angle's curves.
  - The kinking resistance of the distal end should be measured between the 10th mm of the distal end and the first connection point from the distal end.
  - The kinking resistance of the shaft should be measured at two kinking points within its tapered part at least 20-50 mm distance between the kinking points. These points should be not close to the connection points of the guidewire and on thin tapered parts.
  - The kinking resistance of the distal end was characterised by the kinking resistance of the kinking point on the distal end.
  - The kinking resistance of the shaft was characterised by the average kinking resistance of the two kinking points on the shaft.
- In case of guide catheters
  - The kinking angle was the critical kink angle which was shown by the inflection point of diameter change's curve.
  - The kinking resistance should be measured at two points near the distal tip (distance 10-30 mm from the tip, where the kink angle may be different than on the shaft) with minimum 20 mm distance between the bending points on a curvature-free section.
  - The kinking resistance of the guide catheter was characterised by the average kinking resistance of the two kinking points.

Theses (New scientific results)

1. thesis [1,2,3,4,5]

It has been determined that the guidewires' visibility is characterised by the average visibility of the first and last 2 mm (minimum) long part of the radiopaque tip for visibility quantification of straight and pre-formed guidewires, and that it is not necessary to investigate the complete guidewire or distal end. Similarly, the guide catheters' visibility is characterised by the visibility of the marker or the X-ray absorbing on the guide catheter. In the absence of this section, its visibility is characterised by the average visibility of two parts with minimum 2 mm length on the catheter's part between the atraumatic tip and the first curve. It is not necessary the investigation of the complete guide catheter or distal end. The balloon catheters' visibility is characterised by the average visibility of the balloon markers, and it is not necessary to investigate the whole balloon catheter.

In all these sampling cases, the relative standard deviations (coefficient of variation) were not above 0.2.

2. thesis [6,7]

A measuring device was self-developed, which could easily fix the guidewires to the tensile test machine to measure its flexibility. It was determined by measurements made with it that the flexibility of the guidewire can be characterised by nominal bending stiffness. This value describes better it than the force required for to 45o deflection angle of the guidewire (recommended the U.S. Food and Drug Administration).

The nominal bending stiffness is reproducible, but only for measurements at 10 mm distance from the distal end, as it is recommended by the U.S. Food and Drug Administration (5 mm, 10 mm, 20 mm), using centre load.

It was determined that the force required for to 45^{o} deflection angle, is measurable only at this distance using centre load. In case of point load at the free end, this angle is not measurable due to slipping of the guidewire from the load.

3. thesis [8,9,]

The flexibility of the guide catheter is not clearly defined in the literature. Therefore I have determined the inflection point of the dimension change perpendicular to the axis of bending's curve can be characterised by the flexibility of the guide catheter.

It was determined that the behaviour of the bending points along the 120-300 mm section of the investigated guide catheters (irrespective to its diameter) were similar; the difference (which caused deflection angle and dimension change perpendicular to the axis of bending) between the bending points negligible during the flexibility measurement.

Using statistical analysis, it was determined that there are preferred locations (curvature-free parts of the catheter) within this section, where the repeatability of the investigation produced is better results., Therefore, it is better to measure it along those measuring points: one point should be located on 100-200 mm from the distal

end, the other point should be 200-300 mm from the distal end and these two points should be at least 20 mm apart from each other. The mean of the measured values characterises the flexibility of the guide catheter.

4. thesis [10,11]

A measuring device, which is suitable for the objective determination of the guidewire's kinking resistance, was improved. It was determined, that the kinking resistance is different on the main part of the guidewire, on the distal end and on the shaft (irrespective of the degree of the guidewire's flexibility). Therefore this property has to be defined separately.

According to the literature the kinking resistance is the angle, which does not cause permanent deformation yet. This definition was modified: the kinking resistance is the critical kink angle which is shown by the inflection point of measured deflection angle's curve for both distal end and shaft. This value describes better this property.

Using statistical analysis, it was proved that the kinking resistance is reproducible for measurements between the first 10 mm of the distal end and the connection point at the distal end and the shaft.

It was determined that the behaviour of the kink points along the 40-100 mm section of the investigated guidewires (irrespective of the degree of the guidewire's flexibility) were similar; the difference (which caused deflection angle) between the kinking points negligible during the kinking angle measurement. However, there are preferred locations (where there is not connection point in its vicinity and not the thinnest part of the shaft) where repeatability of the investigation is better and hence it is better to measure at these points. The kinking resistance of the shaft should be measured in at two kinking points along the tapered part of the shaft with 20-50 mm distance between the kinking points. The mean of the measured values characterises the kinking resistance of the guidewire shaft.

5. thesis [12,13]

A measuring device, which is suitable for the objective determination of the guide catheter's kinking resistance was improved.

The literature does not contain clear definition to regarding determination of kinking resistance of guide catheters. Therefore, it was determined that the kinking resistance is the critical kink angle which is shown by the inflection point of the dimension change perpendicular to the axis of bending's curve.

Using statistical analysis, it was determined that there are preferred locations (curvature-free parts of the catheter) within the investigated section (10-100 mm from the distal tip), where repeatability of the investigation is better. Therefore, it is better to measure at these measuring points. Its kinking resistance should be measured at two bending points on two curvature-free parts near the distal tip (placed 10-30 mm from the tip, the kink angle may be different than on the shaft) with minimum 20 mm distance between these kinking points. The mean of the measured values characterises the kinking resistance of the guide catheter.

References

[1] S. Moore and S. Ahn, Endovascular Surgery: Expert Consult, Philadelphia: Elsevier Health Sciences, 2010.

[2] M. Kern, The Interventional Cardiac Catheterization Handbook, Philadelphia: Elsevier Health Sciences, 2012.

[3] K. Chatterjee, Cardiology: An Illustrated Textbook, New Delhi: JP Medical Ltd, 2011, p. 521.

[4] R. Morgan and E. Walser, Handbook of Angioplasty and Stenting Procedures, London: Springer-Verlag, 2010, p. 57.

[5] E. Fleck and E. Frantz, Complications in PTCA, Darmstadt: Springer Science & Business Media, 2012, p. 37.

[6] M. Vesely, "When AVF Angioplasty Fails…," *Endovascular Today,* vol. 6, no. 1, pp. 59-65, 2012.

[7] S. Yu, T. Leung, E. Hung, K. Lee and L. Wong, "Angioplasty and stenting for intracranial atherosclerotic stenosis with nitinol stent: factors affecting technical success and patient safety.," *Neurosurgery,* vol. 70, no. 1, pp. 104-113, 2012.

[8] L. Voith, T. Vecsey, L. Major, A. Zsoldos, B. Nagybaczoni, P. Andrássy, K. Zámolyi and J. Tomcsańyi, "Percutaneous coronary intervention without on-site cardiac surgery: the first one thousand patients," *Orv Hetil,* vol. 146, no. 31, pp. 1615-1619, 2005.

[9] R. Azovtsev, V. Sedov, L. Major, I. Gulachi, L. Aleksandrova, V. Pizin and V. Kovalev, "Complications after angioplasty and stenting of coronary arteries in ischemic heart disease patients," *Vestn Khir Im I I Grek,* vol. 161, no. 5, pp. 60-65, 2002.

[10] FDA, "Manufacturer and User Facility Device Experience Database - (MAUDE)," U.S. Food and Drug Administration, 2014. [Online]. Available: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm127891.htm. [Accessed 28 October 2014].

[11] ISO, *Sterile, single-use intravascular catheter introducers,* ISO 11070: 1998, International Organization for Standardization.

[12] ISO, *Sterile single-use intravascular catheters -- Part 1: General requirements,* ISO 10555-1: 2013, International Organization for Standardization.

[13] ISO, *Intravascular catheters -- Sterile and single-use catheters -- Part 4: Balloon dilatation catheters,* ISO 10555-4: 2013, International Organization for Standardization.

Publication of the new results

[1] **L. Pelyhe** and E. Bognár, “Determination of the guidewire’s visibility”. Materials Science Forum. (Submitted)

[2] **L. Pelyhe** and E. Bognár, “Determination of the repeatability and reproducibility of guidewires' visibility measurement”. Journal of Testing and Evaluation. IF: 0.279 (Submitted)

[3] **L. Pelyhe** and P. Nagy, “Relative visibility of diagnostic catheter,” *Acta Polytechnica Hungarica.* (Accepted)

[4] **L. Pelyhe**, P. Nagy and E. Bognár, “Visibility differences within the diagnostic catheter,” in *31th Danubia-Adria Symposium on Advances in Experimental Mechanics*, Düsseldorf, VDI Verein Deutscher Ingenieure e. V., 2014, pp. 84-85.

[5] **L. Pelyhe** and E. Bognár, “Visibility of balloon dilatation catheters,” *Periodica Polytechnica.* (Accepted)

[6] **L. Pelyhe** and A. Kertész, “Flexibility of guidewires,” *Selected Engineering Problems,* vol. 4, pp. 133-138, 2014.

[7] **L. Pelyhe** and A. Kertész, “Vezetődrótok disztális végének flexibilitása,” *Anyagok Világa (Materials Word),* vol. 1, no. 1, pp. 1-7, 2014.

[8] **L. Pelyhe**, A. Kertész and E. Bognár, “Flexibility of diagnostic catheters,” in *Proceedings of XIIIth Youth Simposium on Experimental Solids Mechanics*, Prague, Czech Society for Mechanics, 2014, pp. 84-87.

[9] **L. Pelyhe** and E. Bognár, “Szívkatéterek hajlékonysága, meghajlítása,” *Orvosi Hetilap,* vol. 155, no. 39, p. 1544–1548, 2014.

[10] P. Nagy and **L. Pelyhe**, “Relationship between the kink and the structure of the guidewire,” Periodica Polytechnica Mechanical Engineering, vol. 57, no. 1, pp. 21-25, 2013.

[11] **L. Pelyhe**, M. Bán and E. Bognár, “Kinking resistance of guidewires,” *Materials Science Forum,* vol. 729, pp. 476-481, 2013.

[12] **L. Pelyhe** and E. Bognár, *Kinking resistance of the diagnostic catheters,* Bari: 12. Youth Symposium on Experimental Solid Mechanics, 2013.

[13] **L. Pelyhe** and E. Bognár, “Kinking resistance measurement method for diagnostic catheters”. Innovation and Research in BioMedical engineering. IF: 0.380 (Submitted)

Other publications

[1] Cs. Szalai, I. Ungvári, **L. Pelyhe**, G. Tölgyesi, A. Falus: Asthma from a pharmacogenomic point of view. Br J Pharmacol. 153 (2008:8) 1602-1614 IF: 3,77

[2] **L. Pelyhe**: Investigation of heparin binding capacity of polyurethane coatings. Periodica polytechnica Mechanical Engineering. 54 (2010:2) 95-97.

[3] **L. Pelyhe**: Poliuretánbevonatok heparinmegkötő képességének vizsgálata. Anyagok világa. 9 (2011:2) 1-6

[4] **L. Pelyhe**: Investigation of heparin binding capacity of polyurethane coatings. 28th Danubia-Adria-Symposium on Advances in Experimental Mechanics, 2011.09.28-2011.10.01, Siófok, Hungary, pp. 47-48. (ISBN: 978-963-9058-32-3)

[5] **L. Pelyhe**, E. Bognár, J. Dobránszky: Sztentek funkcionális tulajdonságainak minősítése. VIII. Országos Anyagtudományi Konferencia, 2011.10.09-2011.10.11, Balatonkenese, Magyarország

[6] **L. Pelyhe**, E. Bognár: Kinking resistance of the diagnostic catheters. 12th Youth Simposium on Experimental Solids Mechanics, 21-24 April 2013, Bari, Italy

[7] **L. Pelyhe**, E. Bognár: Vezetődrót röntgensugaras láthatóságának meghatározása. IX. Országos Anyagtudományi Konferencia, 2013.10.13-2013.10.15, Balatonkenese, Magyarország.

[8] **L. Pelyhe**, A. Kertész, E. Bognár: Flexibility of diagnostic catheters. 13th Youth Simposium on Experimental Solids Mechanics, 28 Juny-02 July 2014, Decin, Czech Republic.

[9] **L. Pelyhe**: Stent-development and Beyond. 39th Seminar: Material sciences and biotechnology - Engineers in the healthcare. 12th November 2013, Budapest, Hungary, pp. 48.