2021

Neurovascular Catheter Measurement System Development for Process and Design Effect Evaluation

Cathal Tadhg Merz
Department of Mechanical, Biomedical & Manufacturing Engineering, Munster Technological University, Cork, Ireland, cathal.merz@mycit.ie

Follow this and additional works at: https://sword.cit.ie/allthe

Part of the Biomedical Engineering and Bioengineering Commons

Recommended Citation

This Master Thesis is brought to you for free and open access by the Dissertations and Theses at SWORD - South West Open Research Deposit. It has been accepted for inclusion in Theses by an authorized administrator of SWORD - South West Open Research Deposit. For more information, please contact sword@cit.ie.
Neurovascular Catheter Measurement System Development for Process and Design Effect Evaluation

Cathal Merz
Masters by Research in Engineering, 2021
Department of Mechanical, Biomedical and Manufacturing Engineering

Dr. Gareth O’Donnell, Prof. Ger Kelly
Submitted to Munster Technological University, Jan 2021.
Abstract

Neurovascular guide catheters are used to treat problems affecting blood vessels within the brain through minimally invasive procedures. Catheters are inserted into the patient via their femoral or brachial arteries and manually navigated to the brain to deliver treatment. This procedure replaces the requirement to cut into the patient’s skull and brain tissue but is limited by reduction of blood vessel lumen diameter and increase in tortuosity of blood vessels deep in the brain. During these procedures, catheters can sometimes fail by kinking or fracturing into two pieces.

The rate of failure by fracture of a particular neurovascular catheter device is seen as unacceptably high by its manufacturer. Investigation into the cause of this failure has been carried out using test methods performed by hand. However, these test methods are not standardised and are largely based on the intuition or expertise of the person carrying out the test. Nevertheless, these tests are commonly used as there are no international standards for measuring the mechanical properties of neurovascular catheter shafts.

The aim of the current research is to address this discrepancy in the biomedical device industry by developing a standardised measurement system to replace the manual test methods. The most significant contribution from this research is the fulfilment of this aim. The resulting measurement system can be used to quantify the effect of process and design changes on catheter performance, aiding in the development of better performing, next generation neurovascular catheters to be used in future cutting-edge surgeries. It is the first of its kind to achieve sensitivity great enough to quantify the effect of varying lamination temperature on the catheter’s resistance to kinking. This measurement system was developed using materials testing frames, preconditioning of specimens, micro-CT imaging, DOE, ANOVA, and t-tests.

Additional outcomes from this research are review of applicability of simple tensile, buckle, three-point bend tests and four-point bend tests for the measurement of the effect of varying lamination temperature on the catheter’s resistance to kinking. Additionally, the sequence of events within the neurovascular catheter structure leading to failure have been identified.
Declaration

I declare that this thesis is entirely my own work except where otherwise accredited. It has not been submitted in whole or in part for an award at any other institution.

Mr. Cathal Merz

Dr. Gareth O’Donnell

Prof. Ger Kelly

Jan 2021
Acknowledgements

I would like to thank my family and friends for their enthusiastic motivation throughout my undertaking of this work.

I would also like to thank my Project supervisors, Dr. Gareth O’Donnell and Prof. Ger Kelly of Cork Institute of Technology for their expert advice, mentoring and assistance throughout the duration of this research project without which completion of this work may not have been possible.

I would also like to extend my gratitude toward Cyril Tuohy, Larry Cabellero, Annabel Cooney, Cormac O’Keefe and Dermot Dunne of biomedical engineering excellence who generously gave their time and patience to providing guidance and support whenever sought.
Contents

Abstract ....................................................................................................................... i

Declaration ................................................................................................................ ii

Acknowledgements ................................................................................................... iii

Table of Figures ........................................................................................................ viii

Table of Tables ........................................................................................................ xiv

Publications ............................................................................................................... xv

Nomenclature and Abbreviations .............................................................................. xvi

1 Introduction ........................................................................................................... 1

2 State of Current Industrial Practice ...................................................................... 5

  2.1 Manufacture of Cat. A ......................................................................................... 5

     2.1.1 Inner Layer and Reinforcement Layer Manufacture ....................................... 5

     2.1.2 Outer Layer Assembly .................................................................................. 6

     2.1.3 Lamination, Hub Moulding, Coating and Quality Control ............................ 7

  2.2 Root Cause Analysis .......................................................................................... 9

  2.3 Fractographic Examination ............................................................................... 11

3 Literature Review .................................................................................................. 13

  3.1 Catheter Use ..................................................................................................... 13

  3.2 Catheter Performance Characteristics .............................................................. 14

  3.3 Catheter Design ................................................................................................ 15

  3.4 Catheter and Tube Test Methods ...................................................................... 17

  3.5 Axial Compression and Bending of Idealised Structures ................................... 19

     3.5.1 Bending ........................................................................................................ 20

     3.5.2 Buckling and Kinking .................................................................................... 21

     3.5.3 Saint-Venant’s Principle .............................................................................. 24

  3.6 Kinking of Thin Walled Tubes ......................................................................... 25

  3.7 Hypothesis Testing ............................................................................................ 27
3.7.1 Two Sample T-Test ........................................................................ 30
3.7.2 Analysis of Variance and Post Hoc Test ........................................ 31
3.7.3 Statistical Power ........................................................................... 35
3.8 Literature Review Conclusions .......................................................... 37
4 Methodology and Approach ................................................................ 38
  4.1 Test Method Selection and Design .................................................... 38
  4.2 Experimental Design ........................................................................ 39
  4.3 Specimen Preparation ....................................................................... 41
5 Measurement System Development ....................................................... 44
  5.1 Kink Diameter Test .......................................................................... 44
     5.1.1 Functionality Experiment ............................................................ 46
  5.2 Tensile Test ...................................................................................... 47
     5.2.1 Functionality Experiment ............................................................ 48
  5.3 Axial Loading Test ............................................................................ 51
     5.3.1 Functionality Experiment ............................................................ 51
     5.3.2 Determination of Sequence of Events Proceeding Kink ............... 53
     5.3.3 Sensitivity Experiment 1 ............................................................... 57
     5.3.4 Sensitivity Experiment 2 ............................................................... 58
  5.4 Three-Point Bend Test ...................................................................... 59
     5.4.1 Functionality Experiment ............................................................ 61
     5.4.2 Sensitivity Experiment 1 ............................................................... 62
     5.4.3 Effect of Preconditioning on Device Performance Experiment ....... 63
     5.4.4 Sensitivity Experiment 2 ............................................................... 67
     5.4.5 Sensitivity Experiment 3 ............................................................... 70
  5.5 Four-Point Bend Test ....................................................................... 71
     5.5.1 Sensitivity Experiment 1 ............................................................... 77
     5.5.2 Sensitivity Experiment 2 ............................................................... 78
Analysis and Discussion ........................................................................................................ 80

Conclusions .......................................................................................................................... 83

Appendix A: Experiment Data Statistics and Results.......................................................... 1
  Kink Diameter Functionality Experiment ........................................................................... 1
  Axial Loading Functionality Experiment ............................................................................ 2
  Axial Loading Sensitivity Experiment 1 ........................................................................... 4
  Axial Loading Sensitivity Experiment 2 ........................................................................... 6
  TPB Functionality Experiment ......................................................................................... 8
  TPB Sensitivity Experiment 1 .......................................................................................... 9
  TPB Sensitivity Experiment 2 ........................................................................................ 11
  Effect of Preconditioning on Device Performance Experiment ........................................ 13
    Two Sample T-Test for Max Force ................................................................................ 13
    Two Sample T-Test for Disp. At Kink ......................................................................... 14
    Two Sample T-Test for Force at Kink ........................................................................ 14
    Two Sample T-Test for Displacement at Max Force ...................................................... 16
    Two Sample T-Test for Bending Stiffness Measurement ............................................... 17
  TPB Sensitivity Experiment 2 with Corrected Data ......................................................... 18
  TPB Sensitivity Experiment 2 T-Test ................................................................................... 19
  TPB Sensitivity Experiment 3 .......................................................................................... 20
  FPB Sensitivity Experiment 1 ........................................................................................ 22
  FPB Sensitivity Experiment 2 ........................................................................................ 23

Appendix B: Experiment Settings ....................................................................................... 1
  General Procedures ........................................................................................................... 1
    Apparatus ....................................................................................................................... 1
    Test Programme ............................................................................................................ 1
  Equipment Set-Up ........................................................................................................... 2
  Test Procedure ................................................................................................................. 2
Table of Figures

Figure 1 - Representation of Cat. A considered in this research showing the different layers and diameters. ................................................................. 1
Figure 2 - Locations of proximal and distal ends of a neurovascular catheter as well as proximal, mid and distal shafts. ................................................................. 1
Figure 3 - Kink (left) and fracture (right) on the proximal shaft of a Cat. A device. ...... 2
Figure 4 - “Kink by hand” test performed on the proximal shaft of a Cat. A device. ...... 3
Figure 5 - Parts of the catheter considered in this research.......................................... 5
Figure 6 - Joining process for tube onto substrate such as tube made from polymer with high bending stiffness onto inner layer. ............................................................ 6
Figure 7 - Joining process for tube 1 and tube 2 using hot air. ...................................... 7
Figure 8 - Simplified representation of Cat. A device before the overall outer layer assembly manufacturing step. ................................................................. 7
Figure 9 - Rate of failure by fracture for different catheter designs and products. ........ 9
Figure 10 - Fish-bone diagram showing parameters investigated in root cause analysis for fracture occurrence. The parameters in red were found to affect the rate of fracture occurrence. ................................................................. 10
Figure 11 - Effect of varying lamination temperature on rate of fracture occurrence established using the “kink by hand” test method. ................................. 10
Figure 12 - Kink test method described by A. Bailly et al. [27]....................................... 17
Figure 13 - Sign convention for bending moment. ........................................................ 19
Figure 14 - Deflection of a cantilever beam [23].......................................................... 20
Figure 15 - Buckling of an idealised structure [23]...................................................... 22
Figure 16 - Ideal column with pinned ends (a), with deflected shape (b) and with axial force and bending moment (c) [23]........................................... 23
Figure 17 - Straight, idealised column (a) deflected shape for n = 1 (b) and deflected shape for n = 2 (c) [32]............................................................... 24
Figure 18 - Illustration of Saint-Venant’s Principle [33]............................................. 25
Figure 19 - An infinitesimally small section of an initially straight tube under global bending. Stress components which cause ovalization of the cross section are shown [37]. ........................................................................................................ 26
Figure 20 - Unrotated section of initially straight tube showing components of compressive and tensile forces that ovalize the cross-section. ......................... 26
Figure 46 - Micro-CT images of the Cat. A specimen tested to kink in x-x (left) and y-y (right) planes showing delamination of the different layers from each other. .......................... 56
Figure 47 - Image generated from micro-CT data in the z-z (left) and x-x planes showing plastic deformation of the reinforcement layer. ................................................................. 56
Figure 48 - Boxplot of results from axial loading sensitivity experiment 1. ................ 58
Figure 49 - Boxplot of results from axial loading sensitivity experiment 2. ........... 59
Figure 50 - Three-point bend test fixture. .................................................................. 61
Figure 51 - Boxplot of results from TPB functionality experiment. .......................... 62
Figure 52 - Boxplot of results from TPB sensitivity experiment 1. ......................... 63
Figure 53 - Mandrel used to bend specimen (left) and specimen being bent around mandrel (right) during the preconditioning stage............................................. 64
Figure 54 - Example of plastic deformation on outer layer of test specimen due to preconditioning process. ................................................................. 64
Figure 55 - Significant delamination of Cat. A layer’s after preconditioning. ........... 65
Figure 56 - Boxplot of results from effect of preconditioning experiment ................ 66
Figure 57 - Boxplot of results from TPB sensitivity experiment 2 ......................... 68
Figure 58 - Effect of laminator machine on bending stiffness measurement of nominal samples. ................................................................. 69
Figure 59 - Boxplot of results from TPB sensitivity experiment 2 with corrected data. 69
Figure 60 - Boxplot of results from TPB sensitivity experiment 3 ............................ 71
Figure 61 - Loading diagrams outlined in ASTM d6272 [78]. ................................. 72
Figure 62 - Rudimentary FPB test arrangement showing deformation not consistent with pure bending................................................................. 73
Figure 63 - Deformed Cat. A specimen after rudimentary FPB test .......................... 73
Figure 64 - Reduced anvil diameter FPB fixture. ...................................................... 74
Figure 65 - Collapse of Cat. A specimen under the loading anvil during preliminary FPB testing .................................................................................. 74
Figure 66 - Solid model of the optimised FPB test fixture (left) and FPB test set-up (right). .................................................................................. 75
Figure 67 - Features of the support anvil which aid in alignment with the pneumatic grips. These features are also present on the loading anvil................................. 76
Figure 68 - Alignment tool shown with upper and lower anvils. .............................. 77
Figure 69 - Boxplot of results from FPB sensitivity experiment 1 ............................ 78
Figure 70 - Boxplot of results from FPB sensitivity experiment 2 ......................... 79
Figure 71 - Individual value plot of pooled SD of experiments with lamination temperature as variable. ................................................................. 80
Figure 72 - Individual value plot of mean interval of experiments with lamination temperature as variable. ................................................................. 81
Figure A1 - Power curve for kink diameter functionality experiment.................. 2
Figure A2 - Power curve for axial loading functionality experiment .................... 4
Figure A3 - Force/displacement graph from axial loading functionality experiment 1 based on raw data. Two black markers exist for each specimen, one at the maximum force point and the other at the kink point........................................... 4
Figure A4 - Power curve for axial loading sensitivity experiment 1 ....................... 6
Figure A5 - Power curve for axial loading sensitivity experiment 2 ....................... 7
Figure A6 - Power curve for TPB functionality experiment.............................. 9
Figure A7 - Power curve for TPB sensitivity experiment 1............................... 11
Figure A8 - Power curve for TPB sensitivity experiment 2............................... 12
Figure A9 - Boxplot of max force result from effect of preconditioning experiment. ... 13
Figure A10 - Boxplot of disp. at kink result from effect of preconditioning experiment. ........................................................................................................ 14
Figure A11 - Boxplot of force at kink result from effect of preconditioning experiment. ........................................................................................................ 15
Figure A12 - Boxplot of disp. at max force result from effect of preconditioning experiment........................................................................................................ 16
Figure A13 - Power curve for TPB sensitivity experiment 2 with data corrected. ..... 19
Figure A14 - Power curve for TPB sensitivity experiment 3............................... 21
Figure A15 - Power curve for FPB sensitivity experiment 1............................... 23
Figure A16 - Power curve for FPB sensitivity experiment 2............................... 24
Figure B1 - General naming format for files saved from test............................... 3
Figure B2 - Prototype axial loading test fixture (left) and optimised axial loading test fixture (right)............................................................................................... 5
Figure B3 - Three-point bend fixture................................................................... 6
Figure B4 - Optimised four-point bend fixture................................................... 6
Figure C1 - Naming format for files saved from test......................................... 3
Figure D1 - The SEM examination of specimen 1 identified the presence of two crack initiation zones. The areas imaged at higher magnification are indicated [8]. .......... 1
Figure D2 - SEM image of specimen 1, area 1 at higher magnification. Area 1 corresponds to a crack origin positioned within the middle of the extrusion wall. The crack origin corresponds to a discontinuity resulting from the edge of the reinforcement layer. The crack origin exhibits a relatively smooth morphology with some signs of micro ductility [8].

Figure D3 - SEM image of specimen 1, area 2 at higher magnification. Area 2 corresponds to a second crack origin. The features indicate crack initiation in the mid-wall of the extrusion at the interface between the reinforcement and outer layers [8].

Figure D4 - SEM image of specimen 1, area 3 which corresponds to a union of the two cracks originating at area 1 and area 2 [8].

Figure D5 - SEM image of specimen 1, area 4 which corresponds to the second union of the two cracks originating at area 1 and area 2 [8].

Figure D6 - The SEM examination of specimen 2 identified a single crack initiation zone on the outside diameter on the outer layer (area 1). The areas imaged at higher magnification are indicated [8].

Figure D7 - Image shows specimen 2, area 1, the crack initiation zone at higher magnification. The crack origin exhibits characteristics of mechanical overload. Evidence of micro ductility is present [8].

Figure D8 - SEM image showing specimen 2, area 2. The features are indicative of counter-clockwise crack propagation and the groove in the material represents the interface between the reinforcement layer and outer layer [8].

Figure D9 - SEM image showing specimen 2, area 3, the second mid-fracture location. The features are indicative of clockwise crack propagation [8].

Figure D10 - SEM image showing specimen 2, area 4 which is another mid-fracture location. Some localized deformation is present associated with overload [8].

Figure D11 - SEM image showing specimen 2, area 5, the final fracture zone. A crack union associated with localised mechanical overload is present. Substantial ductility in the form of deformation is evident [8].

Figure D12 - The SEM examination of specimen 3 identified the presence of two crack initiation sites (area 1 and area 2) that are close together. The areas imaged at higher magnification are indicated [8].

Figure D13 - SEM image of specimen 3 showing area 1 and area 2. These areas represent the crack origin [8].
Figure D14 - Higher magnification of specimen 3, area 1. The crack initiated at the interface between the reinforcement layer and the outer layer [8].

Figure D15 - Higher magnification of specimen 3, area 2, the second crack initiation site. The crack initiated at the interface between the reinforcement layer and the outer layer [8].

Figure D16 - Specimen 3, area 3 shows localised ductility from removal of the reinforcement layer during failure [8].

Figure D17 - SEM image showing specimen 3, area 4 which displays minimal evidence of micro ductility [8].

Figure D18 - SEM image showing specimen 3, area 5 indicated by yellow. Some evidence of micro ductility is present [8].

Figure D19 - SEM image showing specimen 3, area 6, the final fracture zone corresponding to a union between the clockwise and counter-clockwise crack propagation. Substantial ductility is present in the form of deformation [8].

Figure E1 - Best presentation award certificate.

Figure F1 - Instron 3345 universal testing system [68].

Figure F2 - Instron 5564 load frame [84].

Figure G1 – Axial Loading Test Fixture Assembly Drawing.

Figure G2 – Axial Loading Test Fixture Assembly Exploded View Drawing.

Figure G3 - Bearing Housing Drawing.

Figure G4 - Winged Nut Drawing.

Figure G5 - Pin Drawing.

Figure G6 - FPB Fixture Assembly Drawing.

Figure G7 - FPB Loading Anvil Drawing.

Figure G8 - FPB Support Anvil Drawing.

Figure G9 - Alignment Tool Drawing.
Table of Tables

Table 1 - Values to be increased (↑) and decreased (↓) in order to maximise torqueability, trackability and pushability of a catheter design according to formulas 1 to 5..............16
Table 2 - Effect of number of groups on the amount of comparisons that are made and family error rate [48]..........................................................29
Table 3 - Calculation of the level of significance to be used in Tukey post hoc test.....34
Table 4 - Example results for Tukey Post Hoc test..............................................35
Table B1 - Settings for axial loading experiments..............................................4
Table B2 - Settings for three-point bend experiments. ......................................5
Table B3 - Settings for four-point bend experiments. ......................................6
Table F1 - Load Cells used throughout research [65, 74]..................................1
Table F2 - Instron test frame displacement rates [68, 83].................................1
Publications

Findings generated by this research up to the three-point bend test arrangement were published in the conference proceedings from the International Conference on Biotechnology, Bioengineering and Biological Solutions held in Barcelona, February 2020 in academic paper format. The author presented the paper at this conference in person and was awarded the best presentation award from the event.

### Nomenclature and Abbreviations

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>Meaning</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>↓</td>
<td>Decrease</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Area</td>
<td>m²</td>
</tr>
<tr>
<td>c</td>
<td>Number of comparisons</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Constant</td>
<td></td>
</tr>
<tr>
<td>df₁</td>
<td>Degrees of freedom associated with $MS_b$</td>
<td></td>
</tr>
<tr>
<td>df₂</td>
<td>Degrees of freedom associated with $MS_w$</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Elastic modulus</td>
<td>N/m²</td>
</tr>
<tr>
<td>F</td>
<td>Force</td>
<td>N</td>
</tr>
<tr>
<td>G</td>
<td>Shear modulus</td>
<td>N/m²</td>
</tr>
<tr>
<td>h</td>
<td>Height</td>
<td>m</td>
</tr>
<tr>
<td>$H_0$</td>
<td>Null hypothesis</td>
<td></td>
</tr>
<tr>
<td>$H_1$</td>
<td>Alternate hypothesis</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Second moment of area</td>
<td>m⁴</td>
</tr>
<tr>
<td>ID</td>
<td>Inner diameter</td>
<td>m</td>
</tr>
<tr>
<td>J</td>
<td>Polar second moment of area</td>
<td>m⁴</td>
</tr>
<tr>
<td>$K_{flexural}$</td>
<td>Flexural spring constant</td>
<td>N/m</td>
</tr>
<tr>
<td>$K_{long}$</td>
<td>Longitudinal spring constant</td>
<td>N/m</td>
</tr>
<tr>
<td>$K_{torque}$</td>
<td>Torsional spring constant</td>
<td>N·m/radian</td>
</tr>
<tr>
<td>M</td>
<td>Bending moment</td>
<td>N·m</td>
</tr>
<tr>
<td>m</td>
<td>Number of sample groups</td>
<td></td>
</tr>
<tr>
<td>MS</td>
<td>Mean squares</td>
<td></td>
</tr>
<tr>
<td>$MS_b$</td>
<td>Mean squares between</td>
<td></td>
</tr>
<tr>
<td>$MS_w$</td>
<td>Mean squares within</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>Number of half cycle sine waves</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>Number of data points in a sample group</td>
<td></td>
</tr>
<tr>
<td>$N^*$</td>
<td>Number of data points excluded from analysis</td>
<td></td>
</tr>
<tr>
<td>OD</td>
<td>Outer diameter</td>
<td>m</td>
</tr>
<tr>
<td>p</td>
<td>Intensity of distributed load</td>
<td></td>
</tr>
<tr>
<td>q</td>
<td>Studentised range statistic</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>Span of supporting anvils</td>
<td>m</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
<td></td>
</tr>
<tr>
<td>$SD_p$</td>
<td>Pooled standard deviation</td>
<td></td>
</tr>
<tr>
<td>SS</td>
<td>Sum of squares</td>
<td></td>
</tr>
<tr>
<td>$SS_b$</td>
<td>Sum of squares between</td>
<td></td>
</tr>
<tr>
<td>$SS_t$</td>
<td>Total sum of squares</td>
<td></td>
</tr>
<tr>
<td>$SS_w$</td>
<td>Sum of squares within</td>
<td></td>
</tr>
<tr>
<td>v</td>
<td>Displacement of a point in the y direction</td>
<td>m</td>
</tr>
<tr>
<td>V</td>
<td>Shear force</td>
<td>N</td>
</tr>
<tr>
<td>x</td>
<td>Displacement in the x direction</td>
<td></td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>Sample mean</td>
<td></td>
</tr>
<tr>
<td>$\overline{x}$</td>
<td>Grand mean</td>
<td></td>
</tr>
</tbody>
</table>
\( x_{ij} \)  
Value of the \( i \)th observation at the \( j \)th sample

\( \bar{x}_j \)  
Mean of the observations at the \( j \)th sample

\( \alpha \)  
Level of significance

\( \mu \)  
Population mean

\( \mu_j \)  
Population mean for the \( j \)th sample

\( \pi \)  
Pi

\( \lambda \)  
Non-centrality parameter

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D</td>
<td>Three-dimensional</td>
<td></td>
</tr>
<tr>
<td>Adj/adj</td>
<td>Adjusted</td>
<td></td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
<td></td>
</tr>
<tr>
<td>ASTM</td>
<td>American Society for Testing and Materials</td>
<td></td>
</tr>
<tr>
<td>Cat</td>
<td>Catheter</td>
<td></td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
<td></td>
</tr>
<tr>
<td>DF</td>
<td>Degrees of freedom in the source</td>
<td></td>
</tr>
<tr>
<td>FEP</td>
<td>Fluorinated ethylene propylene</td>
<td></td>
</tr>
<tr>
<td>FPB</td>
<td>Four-point bend</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
<td></td>
</tr>
<tr>
<td>ISO</td>
<td>International organization for standardization</td>
<td></td>
</tr>
<tr>
<td>Lam</td>
<td>Lamination</td>
<td></td>
</tr>
<tr>
<td>LDPE</td>
<td>Low-density polyethylene</td>
<td></td>
</tr>
<tr>
<td>PTFE</td>
<td>Polytetrafluoroethylene</td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>First quartile</td>
<td></td>
</tr>
<tr>
<td>Q2</td>
<td>Second quartile</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>Third quartile</td>
<td></td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research and development</td>
<td></td>
</tr>
<tr>
<td>RHV</td>
<td>Rotating haemostasis valve</td>
<td></td>
</tr>
<tr>
<td>SE</td>
<td>Standard error</td>
<td></td>
</tr>
<tr>
<td>SEM</td>
<td>Scanning electron microscope</td>
<td></td>
</tr>
<tr>
<td>Temp</td>
<td>Temperature</td>
<td>°C</td>
</tr>
<tr>
<td>TPB</td>
<td>Three-point bend</td>
<td></td>
</tr>
<tr>
<td>vs</td>
<td>Versus</td>
<td></td>
</tr>
</tbody>
</table>
1 Introduction

Thin walled coil reinforced laminate tubes are commonplace in the modern world with popular applications being in oil and gas, electrical and biomedical device industries. The thin walled coil reinforced laminate tube considered in this research is the proximal shaft of a neurovascular catheter (Cat.) referred to as “Cat. A” throughout. Cat. A belongs to a product family which also includes Cat. B and Cat. C, both of smaller inner diameter (ID). Cat. A has a structure consisting of a low-friction polymer inner layer, a nitinol ribbon reinforcement layer, an outer layer made up of multiple sections of polymer to give variable bending stiffness along its length and lastly a hydrophilic outer coating. During manufacture, these three layers are heated and pressed together in an elevated temperature lamination process. These catheters are used in the treatment of stroke which is the third leading cause of death in Ireland [1]. Figure 1 represents the structure and diameters of the proximal segment of Cat. A and Figure 2 shows the terminology associated with different parts of a catheter device.

![Figure 1 - Representation of Cat. A considered in this research showing the different layers and diameters.](image1)

Red - Outer layer (OD = 2.16 mm)
Green - Reinforcement layer
Blue - Inner layer (ID = 1.72 mm)

![Figure 2 - Locations of proximal and distal ends of a neurovascular catheter as well as proximal, mid and distal shafts.](image2)
As a catheter is advanced through tortuous blood vessels in a patient, axial loads may increase gradually or suddenly which can result in failure by kinking and less frequently in failure by fracture. These types of failures as shown in Figure 3 occur most frequently on the devices proximal shaft. Failure by fracture can have catastrophic consequences on a patient as open surgery may need to be performed to remove the broken device. Failure of the device also damages the reputation of the manufacturer.

Figure 3 - Kink (left) and fracture (right) on the proximal shaft of a Cat. A device.

Failure by fracture on the proximal shaft of the Cat. A device occurs at a concerning rate according to its manufacturer. As part of an effort to mitigate the cause(s) for fracture in the device, a study into which process and design parameters effect the rate of occurrence of fracture were carried out by the manufacturer. The results of the study identified that increasing the lamination temperature used during the lamination process caused an observable increase in the rate of fracture of the catheter proximal shaft. This is discussed more in Section 2.2 Root Cause Analysis.

The study carried out by the manufacturer was completed using manually performed qualitative test methods. The first manual test known as the “kink by hand” test is shown in Figure 4 and is executed by holding an approximate gauge length of 30 mm at either end between thumb and forefinger with ends free to rotate. Ends are left free to rotate to remove loading at this location. Next, the operator brings one of their hands rapidly towards the other, forcing the sample to kink. The operator repeats this motion on successive samples with the number of fractures that occur expressed as a percentage. The second manual test is the “wrap” test. This test consists of wrapping a specimen of approximately 200 mm in length around a diameter 12.7 mm mandrel. Results are expressed in the same way as the “kink by hand” test.
These test methods are not fit for purpose. There are unavoidable challenges with controlling the rate of displacement, force applied and alignment as they are dependent on the skill and experience of the operator carrying out the test. Additionally, as these methods produce binary attributive data, the effect of varying a design or process factor on the devices resistance to kinking and/or fracture is difficult to quantify. Despite these serious issues, use of this type of manual testing is common practise as there are no standardised measurement systems for determining mechanical properties of catheter tubes other than tensile strength [2]. Requirements for tensile strength of each cross section and junction with outer diameter greater or equal to 0.55 mm are described in ISO 10555 “Intravascular catheters - Sterile and single-use catheters - Part 1: General requirements”. However, this standard is defined for lengths of catheter shaft with changes in diameter i.e. not constant shaft such as the proximal segment of Cat. A where failure is occurring [3].

The aim of this research is to develop a measurement system to replace the non-standardised, manual test methods. The measurement system is to produce quantitative results for evaluating the effect of process and design changes on the Cat. A proximal shaft. The criterion for sensitivity is such that there is a statistically significant difference in results from high, nominal and low lamination temperature samples. This is based on the root cause analysis carried out by the manufacturer (presented in Section 2.2) which shows an increase in fracture occurrence with lamination temperature. This relationship has been demonstrated repeatedly in practice but thorough investigation into its cause could not previously be carried out due to the shortcomings of the manual test methods. Satisfying required criteria for sensitivity would indicate that the measurement system is
precise enough to study how temperature is affecting properties of the catheter proximal shaft. These results in quantitative form would also represent a massive, tangible improvement over the manual test methods. Fulfilment of the project aim has significant, positive implications for the medical device industry.

The contents of this thesis chart the development of such a measurement system. This is achieved through literature review on catheter use, manufacture, appropriate failure theories and statistical methods for data analysis. The methodology for measurement system development as informed by the literature review, is described in detail and its application to develop the measurement system is described. The measurement system designed and developed by the author comprises of a four-point bend (FPB) test system adapted and re-designed from the plastics industry.
2 State of Current Industrial Practice

This chapter reviews the current manufacturing processes associated with the Cat. A device as well as investigative work carried out by the device’s manufacturer into identifying the causes of fracture in the device.

2.1 Manufacture of Cat. A

This section describes the current processes used to manufacture the Cat. A device. Some of the terminology associated with the Cat. A device and used in this section are shown in Figure 5. Its purpose is to introduce and explain manufacturing processes that are referred to throughout this thesis such as the winding and vertical lamination processes. Through the description of its manufacture, a comprehensive understanding of the structure of the device is also conveyed.

![Figure 5 - Parts of the catheter considered in this research.](image)

2.1.1 Inner Layer and Reinforcement Layer Manufacture

Polytetrafluoroethylene (PTFE) is used for the inner layer of the catheter due to its low coefficient of friction which increases the ease in which other devices and materials can be inserted and withdrawn from the catheter during a medical procedure. The PTFE liner is manufactured and supplied by an external vendor and is film-cast onto a silver-plated, copper core mandrel. A polymer with high bending stiffness relative to the assembled catheter shaft is joined with the proximal end where the hub will eventually be moulded. This is to ensure that the internal diameter (ID) of the device is not deformed during the moulding process which takes place later. The joining process is shown in Figure 6 where the “substrate” is the inner layer and the “material being fused to substrate” is the polymer with high bending stiffness. The process is as follows: a length of low-density
Polyethylene (LDPE) tubing is placed over the material to be joined to the liner as shown in Figure 6. The LDPE tubing length is to be such that it extends beyond either end of the material being joined. The LDPE tubing is held by hand at both ends and hot air is applied evenly to the area. Once joined, the LDPE tubing is removed carefully by hand using a blade.

![Figure 6 - Joining process for tube onto substrate such as tube made from polymer with high bending stiffness onto inner layer.](image)

On completion of the joining process, the liner is loaded into a winding machine and a single helix, variable pitch, nitinol ribbon reinforcement layer is wound onto it starting at the distal end. Following this, a platinum radiopaque marker is attached to the distal end. This marker provides a reference point to the physician during surgery as the platinum will appear dark in comparison to the patient’s tissue through fluoroscopy.

### 2.1.2 Outer Layer Assembly

The entire outer layer of the catheter comprises of two sections, the variable bending stiffness outer layer and the constant bending stiffness outer layer as shown in Figure 5. The variable bending stiffness outer layer is made from a selection of tubes each with different bending stiffnesses. To manufacture this section of the outer layer, tubes are arranged longitudinally, one against the other in order of lowest to highest bending stiffness on a PTFE rod. The tube with the highest bending stiffness corresponds to the proximal end of the subassembly. A length of LDPE tubing is placed over each joint before being fused together using hot air in a joining process illustrated in Figure 7. This process is similar to the joining process shown in Figure 6. On completion, the PTFE rod is stretched to reduce its outer diameter (OD) and the variable bending stiffness outer layer is removed.
Next, the overall outer layer assembly takes place. The assembled inner layer with reinforcement wind as described in the previous section is inserted into the variable bending stiffness outer layer such that the proximal ends of both sub-assemblies align as shown in Figure 8. As the inner layer with reinforcement wind sub-assembly is longer than the variable bending stiffness outer layer sub-assembly, its distal end remains exposed. This exposed distal end is covered by the constant bending stiffness outer layer which is made up of a single material, polymeric tube also shown in Figure 8. The joint between the constant bending stiffness outer layer and the variable bending stiffness outer layer is fused using the process shown in Figure 7.

Figure 7 - Joining process for tube 1 and tube 2 using hot air.

Figure 8 - Simplified representation of Cat. A device before the overall outer layer assembly manufacturing step.

2.1.3 Lamination, Hub Moulding, Coating and Quality Control
Fluorinated ethylene propylene (FEP) tubing is placed over the entire assembly before laminating. Thus far, this assembly comprises of the inner layer with reinforcement wind and outer layers along its entire length. The FEP tubing aids the lamination process by evenly dispersing the heat and pressure throughout the assembly. A horizontal lamination process is carried out by a semi-automated machine. The machine evenly applies heat and pressure around a small length of the catheter and moves along the section to be
laminated. This particular process starts at the junction between the variable bending stiffness outer layer and the constant bending stiffness outer layer as can be seen in Figure 8 and moves along the device in the direction of the distal end.

Following the horizontal lamination process, a vertical lamination process is carried out along the entire length of the assembly. A weight is attached to the proximal end to keep the units taught and vertical. The unit is loaded into a vertical laminator machine and is fully laminated by a combination of heat and pressure, similar to the horizontal lamination process. The now fully laminated assembly is removed from the machine and the FEP layer is removed by a skiving process. A polymer sleeve is attached to the proximal end of the unit in preparation for the hub moulding process which follows.

A pin is inserted into the proximal end of the unit. This determines the inner dimensions of the hub that will be moulded on to it. Following pin insertion, the unit is loaded into a mould and the hub is injection moulded onto it. Excess plastic is trimmed off the hub. The distal end of the unit undergoes a flexing process which increases its trackability (the term “trackability” is explained in Section 3.2 Catheter Performance Characteristics). A strain relief at the hub/proximal end joint is also attached. This reduces the stress concentration at the junction between catheter shaft and moulded hub.

The device is now nearly complete and must be prepared for coating. A mandrel is inserted in the now nearly complete device and a pin inserted into the distal end to protect the radiopaque marker. The distal end is sealed using LDPE tubing and heat. The unit is then coated in a hydrophilic coating which reduces the friction between the device and blood vessel walls during use. The distal end is trimmed and formed into a taper using a tapered mandrel and heat.

Thorough inspections are carried out throughout the manufacturing process, but a final inspection occurs at this stage of manufacture. If the device passes, it is packaged, sterilised and sent to the customer.

The winding process, vertical lamination process and overall construction of the device are of significant relevance to the thesis.
2.2 Root Cause Analysis

Root cause analysis was carried out by the manufacturer of the *Cat. A* device to investigate which design and process factors influenced the rate of occurrence of failure by fracture. As described in Section 2.1.1, the reinforcement layer of the *Cat. A* device consists of a single helix, variable pitch, nitinol ribbon wind. In an earlier design of this product, this layer was built using two pieces of nitinol ribbon. This design was modified to be manufactured using one piece of nitinol ribbon to remove the stress concentration occurring at the junction between the two nitinol pieces and to increase the manufacturability of the device. It was after this design change that failure by fracture increased to a concerning rate. The “kink by hand” and “wrap” test methods were used to evaluate the new single-piece nitinol design with the results confirming an increase in the occurrence of failure by fracture. The results of this testing are shown in Figure 9 alongside results of testing of the two-piece nitinol *Cat. A* design, *Cat. C*, *Cat. B* and a competitor device.

![Graph showing rate of failure by fracture for different catheter designs and products.](image)

*Figure 9 - Rate of failure by fracture for different catheter designs and products.*

Root cause analysis was carried out to investigate which design and process factors influenced the rate of occurrence of failure by fracture, as illustrated in Figure 10. This was again carried out using the “kink by hand” and “wrap” test methods.
The results of varying the lamination temperature are shown in Figure 11. These results are the most significant from the root cause analysis as there is an observable increase in the rate of fracture of the catheter proximal shaft with lamination temperature. Although the manual test methods have certain limitations, repetition of this part of the study has yielded the same results.

Figure 11 - Effect of varying lamination temperature on rate of fracture occurrence established using the “kink by hand” test method.
It was thought possible by the manufacturer of the *Cat. A* device that the proximal shaft experienced thermal degradation from the higher lamination temperature processing resulting in a decline in its mechanical properties. Thermal degradation of polymers occurs due to the application of heat and is influenced by macromolecular structure, environmental conditions and additives [4, 5]. Furthermore, cracking of the polymer outer layer during use can be indicative of excessive residual stress [6]. These residual stresses form in the polymer outer layer from its melting and solidification during the lamination process [7]. Stress concentrations due to agglomerations of pigment in the outer layer material and mechanical damage sustained to the device parts during manufacture were also considered as possible causes for fracture in the *Cat. A* proximal shaft.

To investigate if these factors are contributing or causing fracture, fractographic examination was carried out on the fracture surface of selected failed specimens as discussed in the following section.

### 2.3 Fractographic Examination

Fractographic examination was carried out by a plastics engineering consultant to investigate if thermal degradation, residual stress, agglomerations in outer later material or prior mechanical damage contribute to the cause of fracture of the *Cat. A* specimens. Another purpose of the examination was to identify the point of fracture initiation and was carried out using a scanning electron microscope (SEM) on high lamination temperature specimens which had failed by fracture (Appendix D: Fractographic Examination).

Visual analysis of specimen 1 revealed two crack initiation sites, both of which were located on the interface between the outer layer and reinforcement layer. It was deduced that the reinforcement layer acts as a stress raiser causing the cracking to initiate as the strength of the outer layer polymer material was exceeded [8] [9].

Cracking in specimen 2 initiated at a single site on the outside diameter of the outer layer. It is most likely that this initiation site occurred at the location of greatest bending and cracking occurred when the strength of the material was exceeded [8]. Specimen 3 revealed a single crack initiation site at the interface between the outer layer and reinforcement layer. It is most likely that this crack was induced in the same manner as specimen 1. In all samples, cracking progressed clockwise and/or counter-clockwise until
catastrophic failure occurred. No evidence was found to suggest that cracking initiated due to thermal degradation as previously thought. Material defects including agglomerations and prior mechanical damage of the device were also ruled out as causes for fracture due to lack of supporting evidence [8].

This chapter has discussed manufacture of the *Cat. A* device and investigative work carried out in the form of root cause analysis and fractographic examination by the devices manufacturer and consultant. The parameter(s) causing fracture in *Cat. A* were not identified from the fractographic examination. However, it is considered by the manufacturer of the *Cat. A* device that a mechanical property related to fracture may be detectable using an appropriate measuring system. Again, this cannot be achieved with the manual destructive test methods used during root cause analysis as they produce binary attributive data and are inherently unreliable. This further reinforces the project aim defined in Chapter 1 Introduction to develop a reliable measurement system capable of producing quantitative results. Further investigation into the causes of fracture in the *Cat. A* proximal shaft could then be carried out. This chapter is of crucial importance to contextualise the proceeding work.
3 Literature Review

Literature review was carried out on neurovascular catheter use, performance characteristics and design followed by test methods which may be applicable to testing of the Cat. A proximal shaft. This is followed by a review of methods for modelling a segment of catheter shaft using idealised bending and buckling theory and statistical methods implemented during measurement system development.

Review of literature from peer reviewed journals specific to testing of neurovascular catheters yields few results. This is despite the catheter market having an estimated global value of 15.9 billion US dollars and currently experiencing year on year growth [10]. As a result, this section draws from peer reviewed journals such as the “Journal of Neurosurgery”, “American Journal of Neuroradiology”, “Retina The Journal of Retinal and Vitreous Diseases”, “Advances in Condensed Matter Physics”, “Journal of Offshore Mechanics and Arctic Engineering” and “International Journal of Pressure Vessels and Piping”. Although these journals are not specific to the topic of this research, there is overlap which is drawn upon to form a foundation from which it can be progressed.

Reference to application of this chapters contents in fulfilment of the project aim is made throughout.

3.1 Catheter Use

Endovascular surgery is a minimally invasive surgical technique used to treat problems affecting blood vessels all over the body. It is the job of an interventional radiologist to use a combination or assembly of sheaths, catheters, diagnostic catheters, guide catheters and guide wires to navigate to the site in need of intervention and deliver treatment with the aid of various imaging modalities. Catheters may be inserted into the patient via the femoral artery in the leg or brachial and radial arteries in the wrist [11]. It is during this step in the procedure that device failure occurs most.

Aneurysms can be treated before causing a haemorrhagic stroke using endovascular coils delivered using endovascular surgery [12]. The coils isolate the intra-arterial blood flow from the aneurysmal sac without disrupting the flow in the parent artery [13]. Packing of coils within the aneurysm occlude it to blood flow and induce thrombosis leading to
reduced blood flow and shear stress on the internal wall of the aneurysm [14]. Atherosclerosis can be treated by percutaneous coronary intervention in which a stent is placed at the site of plaque build-up which re-opens the lumen of the vessel reducing blood pressure [15]. Arteriovenous malformations may be treated by blocking its feeding artery through injecting an embolization agent or delivering embolization coils in a way similar to how they are used on aneurysms [16].

Ischemic stroke can be treated or prevented through another catheter-based procedure known as mechanical thrombectomy. This procedure entails guiding the catheter to a neurovascular clot, retrieving the clot using a coil or stent retriever followed by withdrawing the clot from the blood vessel through the catheter. Such clots can also be removed using catheters by aspiration. This method of treatment removes the clot by applying a negative pressure gradient within the catheter which draws the clot into it and removes it from the patient [17].

Due to the nature by which neurovascular catheters are advanced into and though the human body during the above procedures, torqueability, trackability and pushability are maximised for optimum catheter performance. This is described in more detail in the following section.

3.2 Catheter Performance Characteristics

Catheter performance is often described using terms such as torqueability, trackability and pushability. Torqueability is a measure of a catheters torsional stiffness and often expressed as the ratio between rotation of the proximal end to rotation of the distal end [18]. A ratio of 1:1 is highly desirable as this indicates that a rotation of the proximal end by the physician will result in a rotation of the same angle at the distal end inside the patient. A catheter with this characteristic reduces the amount of experience a physician may need to tactfully operate a catheter. Additionally, a catheter of high torsional stiffness is safer to use as a catheter with low torsional stiffness may store energy along its length before rapidly releasing it, causing its distal end to rotate unexpectedly.

Catheter trackability refers to the characteristics of a catheter that allow it to pass through tortuous blood vessels to the area in need of treatment and is largely determined by the devices flexural spring constant [19]. Good trackability is imperative for successful navigation around difficult anatomy such as the ophthalmic artery [20].
The pushability of a catheter refers to the level of force applied by the physician to advance the catheter to the site in need of treatment [21]. Good pushability corresponds to a small amount of axial force needed to advance the distal tip of the catheter in the patient. This characteristic is related to the catheter’s longitudinal stiffness as well as the frictional resistance between the outer surface of the device and its surrounding environment within the patient.

For optimal ease of use, a catheter should exhibit a good combination of all three of these characteristics which can involve design and process compromises [22].

3.3 Catheter Design

Catheter design performance can be modelled by lumped parameter modelling. The devices’ torqueability, trackability and pushability are modelled using torsional, flexural and longitudinal spring constants respectively. These constants describe the amount of force needed to displace a homogenous, isotropic beam through a unit of displacement and assume that the beam is of a homogeneous material which undergoes small deflections only [18] [23]. This modelling technique is approximate by nature but proves a cost-effective design tool. The effect of friction between the catheter and blood vessels on catheter pushability is not accounted for as it is greatest at large amounts of displacement making it very difficult to model or simulate numerically. The effect of friction is evaluated by a physician who tests prototypes by inserting and navigating them around a physical model of tortuous, blood vessel anatomy. This physical model is made of a material with a coefficient of friction similar to human blood vessels.

\[
J = \frac{\pi}{32} (OD^4 - ID^4) 
\]

\[
I = \frac{\pi}{64} (OD^4 - ID^4) 
\]

\[
K_{torque} = \frac{GJ}{2L} 
\]

\[
K_{flexural} = \frac{3EI}{L^3} 
\]

\[
K_{long} = \frac{EA}{L} 
\]
The polar second moment of area \( (J) \) is a measure of an object’s resistance to torsional deformation and is a function of the object’s shape [24]. The second moment of area \( (I) \) is a measure of an object’s resistance to bending and deflection and is dependent on how the material of the object is dispersed from its centroidal axis [25]. The terms \( OD \) and \( ID \) denote the outer and inner diameter of the catheter. The property \( G \) is known as the shear modulus and is the ratio of shear stress to shear strain determined from a direct shear test [23]. The property \( E \) is elastic modulus and is the ratio of stress to strain determined through a simple tensile or axial loading test. The terms \( L \) and \( A \) are for length and area respectively.

Optimal catheter designs maximise torqueability, trackability and pushability. However, not all can be maximised without compromising at least one other of these properties as illustrated by Table 1. For example, to maximise torqueability, one of the values to be increased is \( OD \), but increasing \( OD \) decreases trackability. Catheter devices are made up of multiple sections so that the torqueability, trackability and pushability of each section can be optimised for the conditions it encounters during use. An example is trackability which ranges from highest at the proximal end to lowest at the distal end, which corresponds to the level of tortuosity these parts of the device encounter during use.

Table 1 - Values to be increased (↑) and decreased (↓) in order to maximise torqueability, trackability and pushability of a catheter design according to formulas 1 to 5.

<table>
<thead>
<tr>
<th>Performance Characteristic</th>
<th>Modelled Using</th>
<th>( OD )</th>
<th>( ID )</th>
<th>( L )</th>
<th>( E )</th>
<th>( G )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torqueability</td>
<td>( K_{\text{torque}} )</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>-</td>
<td>↑</td>
</tr>
<tr>
<td>Trackability</td>
<td>( K_{\text{flexural}} )</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>-</td>
</tr>
<tr>
<td>Pushability</td>
<td>( K_{\text{long}} )</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>-</td>
</tr>
</tbody>
</table>

This section has outlined the main characteristics considered during catheter design and performance. Additionally, a method of modelling sections of catheter shaft using lumped parameter modelling has been reviewed. The key points presented in this section are that design compromises always have to be made which may inadvertently lead to unprecedented failure occurrence such as is the case with the proximal shaft of the Cat. A device.
3.4 Catheter and Tube Test Methods

Testing is an essential part of engineering design and manufacture. Testing must take place at many stages in the process of designing new materials, forming of these materials into components and the assembly of these components into products. Throughout development of the manufacturing processes described in Section 2.1 Manufacture of Cat. A, comprehensive testing was carried out by the manufacturer to ensure the processes produced intended results and that they were stable. Depending on the product type, testing does not always cease at the formation of a new product but may be carried out during a product service life too [26]. Measurement of the mechanical properties of a catheter shaft are imperative for an effectively designed product, however no standardised or published test method for achieving this exists [2]. Also, due to the competitive nature of the neurovascular catheter market, test methods are typically not disclosed by manufacturers to the public. Some test methods relevant to catheter design are described in this section.

A test method in the public domain for measuring a catheters resistance to kinking is described by A. Bailley et al. in which either end of a long catheter specimen are brought together and pulled at constant speed through a slot, as shown in Figure 12 [27]. The reading from the test is the height of the specimen remaining above the slot when kink occurs. This test is similar to the kink diameter test used in the medical device industry and explored in Section 5.1 Kink Diameter Test.

![Figure 12 - Kink test method described by A. Bailly et al. [27]](image-url)
Some relevant test methods for determining the mechanical properties of flexible tubes are presented in ISO 10619-1 “Rubber and Plastics Hoses and Tubing - Measurement of Flexibility and Stiffness” [28]. This standard presents a method similar to the “wrap” test method described in Section 1 Introduction. ISO 178-2 “Plastics - Determination of Flexural Properties” describes in detail the procedures for determining the flexural properties of a preferred test specimen by three-point bend (TPB) testing. Test specimens of rectangular cross section are defined in terms of their own relevant material standard and dimensions of length, breadth and height. The span of the two lower supports and test speeds are also defined [29]. ISO 527-2 “Plastics - Determination of Tensile Properties” contains detailed instructions on how to determine the tensile properties of specimens including for anisotropic specimens with detail comparable to ISO 178-2 [29, 30]. Some of these standards are used to inform the measurement system development carried out in this thesis.
3.5 Axial Compression and Bending of Idealised Structures

This research considers two distinct forms of buckling, one simply termed “buckling” and the other termed “kinking”. The definition of both are described for carbon nanotubes in the paper “Buckling and kinking force measurements on individual multiwalled carbon nanotubes” by K. Jensen et al. Applying the definitions used in this paper to buckling and kinking of a catheter shaft reads as follows: “Buckling occurs when an axial compressive load is applied to a catheter specimen and a relatively constant curvature develops along its length. Kinking occurs when this compressive loads increases until a sharp bend forms at one point along its length” [31]. The development of a relatively constant curvature along the catheter shaft during buckling is dependent on the shaft length. The impact of length on a structures curvature under buckling and how kinking can also occur from excessive bending is discussed in Section 3.5.2 Buckling and Kinking.

This section contains the relevant theory for structures in buckling and structures in bending that fail by mechanical overload or kinking which is the work of Leonard Euler, Jacob Bernoulli and many others. The theory presented applies to ideal structures such that they are homogenous, free from imperfections, linearly elastic, perfectly aligned and undergo small deflections only [23]. Both Sections 3.5.1 Bending and 3.5.2 Buckling and Kinking use the same coordinate systems however the coordinate system used to describe buckling is rotated ninety degrees anti-clockwise. This is to make the description true to a common buckling scenario which is in a slender, vertical and axially loaded column. The bending moment sign convention use is shown in Figure 13.

![Figure 13 - Sign convention for bending moment.](image-url)
3.5.1 Bending

When a cantilever beam is loaded with a positive load at its free end as shown in Figure 14, its axis is deformed into a curve. The differential equations for bending moment ($M$), shear force ($V$) and intensity of distributed load ($p$) at any cross section of this beam are [23]:

$$\frac{EI}{x^2} \frac{d^2 v}{dx^2} = M$$  \hspace{1cm} (6)

$$\frac{EI}{x^3} \frac{d^3 v}{dx^3} = V$$  \hspace{1cm} (7)

$$\frac{EI}{x^4} \frac{d^4 v}{dx^4} = -p$$  \hspace{1cm} (8)

![Figure 14 - Deflection of a cantilever beam [23].](image)

Elastic modulus multiplied by the second moment of area ($EI$) denotes the flexural rigidity for bending in the $x$-$y$ plane and the differential term is the lateral deflection in the $y$ direction of a point, distance $x$ from the origin at point $A$. It is interesting to note that these differential equations apply also to an idealised structure in buckling as discussed in Section 5.4 Three-Point Bend Test. Integration of equation (6) for end conditions associated with simply-supported three-point bending give equations (9) for displacement of a point in the $y$ direction ($v$) [23]:
\[ v = \frac{FL^3}{48EI} \]  

(9)

This formula is applicable to the three-point bend test method used in Section 5.4 for small deflections and may be used to calculate the elastic modulus or flexural rigidity \((EI)\) of the specimen.

3.5.2 Buckling and Kinking

Buckling is an instability that leads to structural failure from kinking. It occurs in axially loaded slender compression members which under an increasing axial load, deflect laterally before complete collapse or kink [23, 31]. As a catheter is being pushed into a patient’s body, it may fail in this way as the combined friction of the patient’s vessels and valve it passes through outside of the patient (known as a RHV) against the catheter creates a force that opposes the axial force applied by the physician.

The fundamental concepts of buckling and stability are described by Stephen P. Timoshenko and James M. Gere in their book “Mechanics of Materials” by considering a vertical slender structure illustrated in Figure 15. The structure is made up of two bars of equal length, connected by a pin at point \(B\) and with both ends pinned. The structure is held in a vertical position by a torsional spring in its central pinned connection and has a compressive load \(F\) acting along its longitudinal axis. The axial load \(F\) has the effect of increasing the lateral displacement of point \(B\) and the rotational spring has the effect of counteracting this displacement. The structure is stable when a relatively small force \(F\) is applied to the structure, point \(B\) displaces laterally but returns to its original position when the force is removed. Under unstable conditions a large force \(F\) is applied and point \(B\) continues to displace laterally until the structure collapses [23].
The solutions for the equation for equilibrium of the structure show that the structure is in equilibrium when there is no displacement and at the critical load. The critical load is the only load for which the structure can be in equilibrium while also having lateral displacement of point $B$. This is because the spring force at point $B$ which acts against the load $F$ are the same. The structure transitions from stable to unstable at the critical load.

Now considering the axially loaded column shown in Figure 16 (c), the bending moment $M$ at the distance $x$ from the origin (corresponding with the lower pinned end) is shown acting in the positive direction with axial force $F$ acting at the same cross section. There are no shear forces in the column as there are no horizontal forces present. Equilibrium of moments about point $A$ gives:

$$M = -Fv$$

(10)

Where $v$ is the displacement of the cross section in the positive $y$ direction. If the column buckled to the opposite side, the same expression for bending moment is obtained as the deflection is negative but the moment about the origin caused by the axial force $F$ changes such that the equilibrium equation for moments about point $A$ result in equation (11) which is the same as (10).

$$M - F(-v) = 0$$

(11)
The differential equation for bending moment of a cantilever beam with a positive load at its free end (equation (5)) is applicable to the column described as it bends as if it were a beam when axial load $F$ is applied [23]. This equation is used to determine the critical load ($F_{crit}$) and corresponding deflected shapes for the column. Substituting equation (11) into equation (6) gives:

$$EI \frac{d^2v}{dx^2} + Fv = 0 \quad (12)$$

The difference between equation (6) and (12) is that in the case of beam deflection, the bending moment ($M$) is a function of the load only and so the equations of equilibrium are not affected by the deflection of the beam. In the case of buckling, the geometry of the displaced structure is considered as the bending moment is a function of the deflected column. The solutions to the differential equation for buckling are [23]:

$$F_{crit} = \frac{n^2\pi^2EI}{L^2} \quad (13)$$

$$v = C \times \sin \frac{n\pi x}{L} \quad (14)$$
The $n$ term is the amount of half cycle sine waves the column forms when deformed by the axial load. The lowest critical load for a column occurs when $n$ is equal to one. The term $C$ is a constant that represents the maximum deflection of each half sine wave of the column as shown in Figure 17. The type of buckling described here is known as Euler Buckling. The critical load can be increased by using a material with higher elastic modulus or second moment of area [23].

![Figure 17](image)

*Figure 17 - Straight, idealised column (a) deflected shape for $n = 1$ (b) and deflected shape for $n = 2$ (c) [32].*

As stated at the beginning of this section, this buckling theory is applicable to how the *Cat. A* device is deforming before failure during use. Furthermore, this theory can be used to describe loading during the axial loading test used in Section 5.3 Axial Loading Test.

### 3.5.3 Saint-Venant’s Principle

Saint-Venant’s Principle so named after Barré de Saint-Venant, a famous French mathematician and elastician, describes the nature of stress concentrations and is based on theoretical and practical experience [23]. It can be illustrated by considering three cross sections $a-a$, $b-b$ and $c-c$ of a linearly elastic, solid bar subject to a concentrated load $F$ at its end as shown in Figure 18.
The maximum stress in the bar reduces as the distance from the point of application of load increases. The peak stress at section $a-a$ is several times higher than the average stress as it is positioned close to the load. The peak stress reduces at cross section $b-b$ and at $c-c$, the stress distribution is uniform.

Saint-Venant’s principle is important to consider in measurement system design. During the experiment, there will be a stress concentration where the specimen is clamped or supported. If the specimen length is too short, the peak stress at the point of specimen failure will overlap with the peak stress caused by clamping or supporting of the specimen. This can introduce variation in experiment results due to the measurement system set-up. Specimen length is chosen such that this does not occur during measurement system development described in Section 5.

3.6 Kinking of Thin Walled Tubes

Kinking of thin walled metal tubes is comprehensively described in “Theory of Elastic Stability” by Stephen P. Timoshenko and James M. Gere, (1961) “Buckling Strength of Metal Structures” by Friedrich Bleich (1952) and “Guide to Stability Design for Metal Structures” edited by Theodore V. Galambos (1998) [32, 34, 35]. It is significantly more difficult to analyse than axial compression and bending of idealised structures described in Section 3.5 Axial Compression and Bending of Idealised Structures. The study of idealised structures in bending and buckling is valuable when considering a large portion of the Cat. A device in bending or compression. However, when considering the area in
which significant deformation occurs in the device, theories associated with kinking are most suitable.

The theory of hollow sections under bending are complex with their analytical treatment having a history going back over a century. L. G. Brazier illustrates a point at which a bending moment applied to a tube passes through a maximum value, after which resistance to bending reduces and failure of the structure occurs [36]. When an initially straight tube is bent uniformly, the longitudinal tension and compression which resist the applied bending moment (shown in Figure 19 in blue and red respectively) have stress components which tend to ovalize the cross-section [37]. These stress components and the direction in which they act are shown in Figure 20. The cross section where kink occurs in the catheter shaft would be subject to similar stresses.

![Figure 19 - An infinitesimally small section of an initially straight tube under global bending. Stress components which cause ovalization of the cross section are shown [37].](image1)

![Figure 20 - Unrotated section of initially straight tube showing components of compressive and tensile forces that ovalize the cross-section.](image2)
As the load is steadily applied, ovalization of the tube increases and flexural rigidity decreases with second moment of area as the material of the structure moves closer to the neutral axis. This is known as the Brazier Effect [38]. After the bending moment reaches its maximum value, the structure becomes unstable and the tube suddenly kinks [38]. It has been shown that kinking of bent elastic long cylinders can be predicted using an ovalized pre-kinked configuration numerical model [39].

Precise mathematical modelling of kinking becomes increasingly difficult when the structures considered are non-homogenous, such as the catheter considered in the current research. Similar challenges are presented in the “Journal of Offshore Mechanics and Arctic Engineering” and “International Journal of Pressure Vessels and Piping” in the analysis of multi-layer, reinforced, flexible pipes which are used in the oil and gas extraction industry [40-42].

In the development of a numerical model for kinking, experimental results are crucially important for validation purposes [43]. Additionally, physical testing must be carried out in the biomedical industry in order to meet industry standards such as the ISO 10555 standard which describes the tensile strength requirements of material junctions along a catheter [3].

Investment in the development of measurement systems for catheter design evaluation is therefore necessary even when numerical simulations are used. If data is collected from test specimens and analysed using the correct statistical methods, statements about the device can be determined to be true or false using hypothesis testing. This is discussed in detail in the following sections.

3.7 Hypothesis Testing

Hypothesis testing is a method used to make statistical decisions with experimental data and quantifies the probability that a sample mean is unusual. A hypothesis test evaluates two mutually exclusive statements about a population known as the null hypothesis ($H_0$) and the alternate hypothesis ($H_1$) to determine which statement is best supported by the sample data [44]. The null hypothesis states that no difference exists between population mean 1 ($\mu_1$) and population mean 2 ($\mu_2$). The alternate hypothesis states that a difference exists between $\mu_1$ and $\mu_2$. 
Hypothesis tests work by taking a test statistic calculated using sample data and comparing it to a value obtained from the appropriate probability distribution associated with the level of significance (\(\alpha\)) of the test [45]. The probability distribution is formed from the probability of all possible outcomes of a random process for a random variable [46]. As the properties of these distributions are well understood, they can be plotted without the need of carrying out multiple experiments assuming that samples are drawn randomly from a population where the null hypothesis is true [45]. Probability distributions can be discrete or continuous depending on the population data they are describing. Continuous probability distributions are used in this research as the data obtained from experiments is continuous.

Hypothesis testing is carried out in this research by means of two sample t-test and one-way analysis of variance (ANOVA). A five percent level of significance (\(\alpha = 0.05\)) is used for this research denoting that there is a five percent risk of a type I error occurring [47]. A type I error is when the null hypothesis is true but rejected. For example, if no actual difference exists between Cat. A specimens manufactured using different manufacturing settings but a difference is incorrectly detected from the test method data. Type II error occurs when the null hypothesis is false but not rejected. An example of this is if an actual difference exists between Cat. A specimens manufactured using different manufacturing settings but none is detected from the sample data.

Two sample t-tests are a type of hypothesis test used to determine if the difference between two sample means is unusual. Two sample t-tests should not be used if there are more than two sample means. The reason for this is that sample means are compared in pairs resulting in the number of comparisons (\(c\)) increasing as illustrated in Table 2 [48]. As there is a probability of making a type I error with every comparison, the overall probability of making a type I error (family error rate) increases to unacceptable levels for the analysis. An appropriate analogy for this is how the chances of rolling one to six
on a six-sided dice is one in six. This probability increases with the number of dice throws until it becomes almost certain that the number will be rolled. The effect of the number of comparisons made for an analysis is illustrated in Table 2 where the family error rate is calculated using formula (17).

Table 2 - Effect of number of groups on the amount of comparisons that are made and family error rate [48].

<table>
<thead>
<tr>
<th>Samples (m)</th>
<th>Comparisons (c)</th>
<th>Family Error Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1</td>
<td>0.05</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>0.142625</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>0.264908109</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>0.401263061</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>0.53670877</td>
</tr>
<tr>
<td>7</td>
<td>21</td>
<td>0.659438374</td>
</tr>
<tr>
<td>8</td>
<td>28</td>
<td>0.762173115</td>
</tr>
<tr>
<td>9</td>
<td>36</td>
<td>0.84220785</td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>0.900559743</td>
</tr>
<tr>
<td>11</td>
<td>55</td>
<td>0.940461445</td>
</tr>
<tr>
<td>12</td>
<td>66</td>
<td>0.966134464</td>
</tr>
<tr>
<td>13</td>
<td>78</td>
<td>0.981700416</td>
</tr>
<tr>
<td>14</td>
<td>91</td>
<td>0.990506054</td>
</tr>
<tr>
<td>15</td>
<td>105</td>
<td>0.995418807</td>
</tr>
</tbody>
</table>

\[
\text{Family error rate} = 1 - (1 - \alpha)^c \quad (17)
\]

One-way ANOVA is used for experiments where there are more than two samples as this method maintains the chance of making a type I error at a constant. One-way ANOVA is used to determine if a statistically significant difference exists between the samples followed by Tukey post-hoc tests to determine between which samples the difference exists [49].

The assumptions made for the two sample t-tests and ANOVA hypothesis tests carried out are as follows [49-52]:

1. That the data is normally distributed.
2. That the samples are random i.e. each data point in the population has an equal chance of being included in the sample.
3. The value of one data point does not influence or affect the value of another, known as independence.
4. That variances are approximately the same across samples.
5. That there are no significant outliers.
6. That the measurement system is accurate, precise and stable.

The assumption of random sampling could not be adhered to as the test specimens are made for the purpose of destructive testing and so are not taken directly from the population through random selection. Additionally, the data does not conform with the assumption of equal variances in some cases however, the conclusions drawn from these experiments with respect to the project aim remain the same.

3.7.1 Two Sample T-Test

As previously stated, a two sample t-test is used to measure if a statistically significant difference exists between two sample means. They are called t-tests as the comparison is made after calculating a statistic known as a t-statistic using formulas (18), (19) and (20) when equal variances are assumed.

\[ t\text{-statistic} = \frac{\bar{x}_1 - \bar{x}_2}{SD} \]  
\[ (18) \]

\[ SD = SD_p \sqrt{\frac{1}{N_1} + \frac{1}{N_2}} \]  
\[ (19) \]

\[ SD_p = \sqrt{\frac{(N_1 - 1)(SD_1^2) + (N_2 - 1)(SD_2^2)}{N_1 + N_2 - 2}} \]  
\[ (20) \]

The t-statistic can be thought of as the signal to noise ratio where the numerator term in formula (18) is the difference between sample means and the denominator term \( SD \) is the estimated standard deviation of the difference between sample means [53]. This term is calculated using the value for pooled standard deviation \( (SD_p) \). A relatively large signal value (numerator) and low noise value (denominator) results in a large t-statistic and indicates how distinguishable the signal is from the noise. Low t-statistics suggest that the observed difference between the sample mean and null hypothesis mean is due to random error.
In order to draw meaningful conclusions from a t-statistic, the concept of t-distributions and t-values must be introduced. The t-distribution is a type of probability distribution that provides hypothesis tests for single means and is defined by the number of independent observations in a sample data set \( N \) [54, 55]. The first step in the process of a t-test is to form the null and alternate hypothesis as per formulas (15) and (16). Secondly, the t-statistic is calculated as per formula (18) and plotted on the t-distribution as shown in Figure 21. The shaded area on the distribution represents the probability of obtaining the t-statistic calculated using the experiment data. This probability can be found using tabulated values for the area under the distribution. If the probability is less than the level of significance, this denotes that the t-statistic is unusual when compared to the population data. The null hypothesis is rejected denoting that a statistically significant difference exists between the two populations.

Two sample t-tests are used in Section 5.4.4 to determine if a statistically significant difference exists between Cat. A specimens manufactured on a R&D laminator machine and a production laminator machine. They are also used to investigate the differences between specimens subjected to preconditioning before testing in Section 5.4.3 Effect of Preconditioning on Device Performance.

3.7.2 Analysis of Variance and Post Hoc Test

One-way ANOVA is used to test the null hypothesis that all group means of a categorical variable are equal. It is used when there are at least three sample groups as two-sample t-test can be used when there are two [56]. In the context of this research, one-way
ANOVA is mostly used to determine if a statistically significant difference exists between three *Cat*. A sample groups each group manufactured differently. To carry out one-way ANOVA, the sum of squares between (*SS*$_b$), sum of squares within (*SS*$_w$) and the total sum of squares (*SS*$_t$), must be calculated using formulas (21), (22) and (23) respectively. If two of these values have been calculated, then formula (24) can be used to calculate the third. *SS*$_w$ and *SS*$_b$ indicate how much of *SS*$_t$ is due to variation within or between sample groups respectively [54].

\[ SS_b = N \sum (\bar{x}_j - \bar{x})^2 \]  

(21)

\[ SS_w = \sum (x_{ij} - \bar{x}_j)^2 \]  

(22)

\[ SS_t = \sum (x_{ij} - \bar{x})^2 \]  

(23)

\[ SS_t = SS_w + SS_b \]  

(24)

The *f*-statistic is the ratio of mean squares for between (**MS**$_b$) and within (**MS**$_w$) values. The mean squares value is equal to the respective sum of squares value divided by the appropriate degrees of freedom. The degrees of freedom describes the number of values in the final calculation of a statistic that are free to vary i.e. how many independent data points are needed to calculate the statistic [57]. The degrees of freedom associated with **MS**$_b$ (df1), is equal to the number of sample groups (m) minus one. This is because in the calculation of *SS*$_b$, if the grand mean is known, then it is only the total number of samples minus one that are needed in order to calculate the statistic. For **MS**$_w$, the degrees of freedom associated with **MS**$_w$ (df2) is the number of data point in each sample minus one, multiplied by the number of samples. Again, this is consistent with the calculation of *SS*$_w$. The *f*-statistic is the ratio of **MS**$_b$ and **MS**$_w$ and calculated as per formulae (25), (26) and (27):
\[ f\text{-statistic} = \frac{MS_b}{MS_w} \] (25)

\[ MS_b = \frac{SS_b}{m - 1} \] (26)

\[ MS_w = \frac{SS_w}{m(N - 1)} \] (27)

Next, the appropriate f-distribution is selected. The f-distribution is defined by the degrees of freedom for \( MS_b \) (\( df_1 \)) and \( MS_w \) (\( df_2 \)) so represents the probability of multiple levels of events in one plot. The f-statistic is plotted on the f-distribution plot and the area to the right of the f-statistic is found using tabulated values for the area under the distribution. This area represents the probability of obtaining the f-statistic and it can be seen that if an f-statistic is large, there is a lower probability that the null hypothesis is correct \[54\]. Figure 22 represents an f-distribution with \( df_1 = 3 \) and \( df_2 = 36 \). The f-statistic associated with the experiment data in this figure data is 3.3, the probability of getting an f-statistic larger than this is equal to 0.03 (the shaded portion of the curve). This is less than the level of significance of 0.05 so the null hypothesis would be rejected in this case.

![F-distribution plot example](image)

Post-hoc tests are carried out after one-way ANOVA has confirmed that a statistically significant difference exists between sample means to determine between which groups
the difference exists. Similar to one-way ANOVA, post-hoc tests control the probability of a type I error occurring. If homogeneity of variances is assumed and sample sizes are approximately equal, Tukey post-hoc test should be used [49].

The Tukey method used in this research compares sample means using a t-test. However, the level of significance for each comparison is chosen such that the family error rate remains at 0.05 [48]. The level of significance to be used for each comparison can be obtained by taking an iterative approach to solving formula (17). The results of such an approach are presented in Table 3 where the number of comparisons is held constant at 3 and the level of significance is reduced from 0.05 in increments of 0.001. In order to maintain a family error rate of 0.05, the level of significance used for each comparison is between 0.014 and 0.019.

<table>
<thead>
<tr>
<th>Level of Significance</th>
<th>Family Error Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.050</td>
<td>0.143</td>
</tr>
<tr>
<td>0.049</td>
<td>0.140</td>
</tr>
<tr>
<td>0.044</td>
<td>0.126</td>
</tr>
<tr>
<td>0.039</td>
<td>0.112</td>
</tr>
<tr>
<td>0.034</td>
<td>0.099</td>
</tr>
<tr>
<td>0.029</td>
<td>0.085</td>
</tr>
<tr>
<td>0.024</td>
<td>0.070</td>
</tr>
<tr>
<td><strong>0.019</strong></td>
<td><strong>0.056</strong></td>
</tr>
<tr>
<td><strong>0.014</strong></td>
<td><strong>0.041</strong></td>
</tr>
<tr>
<td>0.009</td>
<td>0.027</td>
</tr>
<tr>
<td>0.004</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Results of Tukey Post Hoc tests are presented as shown in Table 4. When two samples share a letter in the grouping column, this denotes that no statistically significant difference exists between the means of those samples. The project aim specifies the requirement to measure a statistically significant difference between three sample made using high, nominal and low lamination temperature samples. This would be indicated by results of the post hoc test showing three separate groups A, B and C for each sample.
Table 4 - Example results for Tukey Post Hoc test.

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>9</td>
<td>7.331</td>
<td>A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>9</td>
<td>6.248</td>
<td>B</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>5.747</td>
<td>B</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

3.7.3 Statistical Power

Statistical power is the probability of correctly rejecting the null hypothesis i.e. not making a type II error. Statistical power increases with level of significance, effect size, and sample size [54]. The statistical software used for this research calculates the required sample size for a specified experimental power using an iterative approach. Using data from previous experiments, the user specifies the pooled standard deviation, number of sample groups and the maximum difference between means. The software evaluates the statistical power for a trial sample size until the specified value is reached [59]. These calculations use a non-central f-distribution defined by $df1$, $df2$ and a non-centrality parameter ($\lambda$). The non-centrality parameter is a measure of the probability of the null hypothesis being false [60]. As it increases, the f-distribution shifts to the right increasing the probability of the f-statistic falling into the rejection region of the distribution as shown in Figure 23. This means that there is a higher probability of rejecting $H_0$.

![Figure 23 - Illustration of the effect of increasing the non-centrality parameter (blue) from a central f-distribution (green) [61].](image_url)
The non-centrality parameter and power are calculated as per formulae (28) and (29). The f-value used in formula (29) is that which is associated with the non-central f-distribution, level of significance and degrees of freedom $df1$ and $df2$.

$$\lambda = \frac{2N \times SS_b}{SD_p^2}$$  \hspace{1cm} (28)

$$Power = 1 - f\text{value}$$  \hspace{1cm} (29)

A power curve can be plotted using the level of significance, pooled standard deviation, sample size and number of sample groups. It represents every combination of power and maximum difference between means when these parameters are held constant [62]. An example of a power curve is shown in Figure 24 for sample sizes of 5, 7 and 9. The maximum difference between means is marked on each curve. Power is shown to increase with sample size and maximum difference between means.

![Power Curve for One-way ANOVA](image)

*Figure 24 - Power curve for one-way ANOVA [62].*

In this research, statistical power, level of significance, pooled standard deviation and number of samples are held constant to calculate the sample size required to obtain a statistical power of 0.8. A statistical power of 0.8 is considered adequate for most research applications [63].
3.8 Literature Review Conclusions

This chapter has firstly explored the uses of neurovascular catheter devices giving some context to the circumstances under which failure occurs and how detrimental fracture of the Cat. A device is for the patient. Secondly the main characteristics considered during catheter design and performance were outlined and a method for modelling these characteristics using lumped parameter modelling reviewed. Test methods specifically for catheters which are not standardised and other standardised test methods that may be applicable to the aim of this research are also reviewed. Methods for failure analysis considering the catheter structure as an ideal beam in bending or column in buckling are presented in addition to literature review on kinking and the Brazier effect. Finally, the methods used for statistical analysis of results obtained from test method development carried out during this research are explained and justified.

Points of significance interest that have arisen in this chapter are:

- Design compromises always have to be made i.e. to increase one design characteristic another has to be decreased.
- No standardised test method exists for determining the mechanical properties of catheter shafts.
- According to idealised beam bending and column buckling theory, the differential equation for bending moment of a cantilever beam with a positive load at its free end is applicable to a column in buckling with axial load applied. This suggests that a catheter shaft in bending behaves similarly to when in compression. This is important for test method selection.
- For experiments with two sample groups, data should be analysed using two sample t-tests to determine if a statistically significant difference exists between sample means. For experiments with more than two sample groups, one-way ANOVA with Tukey Post Hoc tests should be used for the same purpose.

The contents of this chapter are beneficial to the understanding and/or rationale used throughout the rest of this thesis.
4 Methodology and Approach

This chapter describes the methodologies and approach taken to develop a measurement system that satisfies the project aim.

4.1 Test Method Selection and Design

The rationale behind initial test method selection is described as follows: Test methods suitable for measuring the mechanical properties of the proximal shaft of Cat. A were selected and adapted for purpose. Their suitability as a design and process change effect measurement tool was assessed by carrying out experiments with the aim of measuring a statistically significant difference between samples made at high, nominal and low lamination temperature settings. If problems with the test methods’ sensitivity or otherwise became apparent, then the next possible solution was investigated and adapted for purpose as informed by previous testing and literature. The measurement system development plan entailed repeating these steps until a test method that was practical, repeatable, reliable and sensitive enough to quantify the effect of design and process changes was developed. This method of test method selection allows for quick iteration of different test methods with the opportunity to apply inventive improvements at each step.

A materials test frame is a machine used mostly to determine the tensile and compressive strength of materials. Use of a materials test frame was identified as advantageous as the user is granted control over the criteria for initiating the test, variables during the test, criteria for ending the test and recording outputs from the test. A test carried out on a test frame would be an improvement on the manual test methods with respect to repeatability, reliability and the types of results obtained i.e. from binary qualitative to quantitative. The experiment readings were chosen as force and displacement. Maximum force, yield point, kink point and bending stiffness measurement can be calculated from these readings. The method of experiment planning used was the one-factor-at-a-time method with the lamination temperature setting being chosen as the first factor to change as this had the most significant effect on fracture occurrence as described in Chapter 1 Introduction.
4.2 Experimental Design

Due to the level of complexity and variability associated with changing a single process or design parameter of Cat. A, one-factor-at-a-time test planning was used. Upon selection of the test configuration, the key variable was chosen. The test parameters investigated during root cause analysis, as discussed in Section 2.2 Root Cause Analysis and shown in Figure 10, informed the variable chosen. Variables investigated over the duration of this work include lamination temperature, reinforcement layer pitch, catheter product and laminator machine.

Most experiments were designed with lamination temperature or reinforcement layer pitch being the key variable. Lamination temperature was chosen as the project aim specifies measurement of a statistically significant difference between units made using differing lamination temperatures as an objective. This is motivated by the relationship obtained through the “kink by hand” test which shows an increase in the rate of fracture with lamination temperature as discussed in Section 2.2. Reinforcement layer pitch was chosen as its effect on the mechanical properties of a helical wind are better understood. An increase in the number of active winds in a given length of catheter shaft effectively increases its elastic modulus [64].

The lamination temperature test samples are described as high, nominal and low. The nominal sample is so named as the lamination temperature is not changed from the manufacturing setting allowing this sample to act as a control. In the case of both lamination temperature and pitch, the experiment variable is varied by the same magnitude from the nominal sample for both the high and low samples as illustrated in Figure 25.

![Graph illustrating the equal difference in experiment variable between samples.](image)

*Figure 25 - Graph illustrating the equal difference in experiment variable between samples.*
The test specimens comprise a shaft of the catheter cut to a specified length. The length of the test specimens is informed by Saint-Venant’s Principle such that the end conditions do not affect the stress conditions at the longitudinal centre of the test specimen, where failure occurs.

For experiments where lamination temperature is varied, the settings for low, nominal and high are 220.56, 232.22 and 243.89 °C respectively. The low temperature is chosen as the melting point of the outer layer to ensure adhesion between the outer layer and the reinforcement layer. The high lamination temperature is chosen such that there is an equal difference between the high and nominal sample and low and nominal sample as per Figure 25.

An iterative approach is used for test method development. Test settings, experiment settings and the fixture design are scrutinised and areas of improvement addressed at each iteration. To ensure informed decision making during the progression of the test method development, control measures were implemented to reduce variability in the test set-up. Additionally, only the significant variable under investigation was varied between catheter sample groups. The Cat. A design variables investigated are the reinforcement layer pitch or lamination temperature settings.

In the context of this research, the experiment carried out using the first iteration test method is named a functionality experiment. The primary aim of the experiment is not to measure a statistically significant difference between samples but to identify areas of improvement for optimisation of the test arrangement. If the results of the functionality experiment display excessive variability or if unavoidable issues with the experiment set-up become apparent, the test method is not iterated further.

Subsequent iterations from the functionality experiment are called sensitivity experiments. The aim of these experiments is to measure a statistically significant difference between sample groups. If proceeding iterations of the sensitivity experiment continue to fail to measure a difference between sample groups, the process starting with a functionality experiment was repeated using a different test method. Selection of the test method was informed by literature review and analysis of previous experiments.

For each experiment, sample group size was initially taken as a best guess as what was required for a statistical power of 0.8. However, where one-way ANOVA was carried out, the results were used to carry out a calculation for statistical power as presented in
Appendix A: Experiment Data Statistics and Results. These results are used to inform the sample group size of proceeding experiments.

4.3 Specimen Preparation

This section describes the process employed for preparation of Cat. A proximal shaft specimens for the test methods described in Section 5 Measurement System Development. For the kink diameter and tensile test methods, condition of the specimen ends does not influence the test readings. This is because for the kink diameter test, the specimen ends are at too great a distance from the area of failure to affect it. For the tensile test, the specimen ends are clamped using grips and so it is the effect of the grips on the specimen that must be mitigated rather than the condition of the specimen ends. For these reasons, steps 1, 3 and 4 do not need to be followed for specimen preparation for these tests. These steps are applicable to specimens used in compression, TPB and FPB testing as irregular ends will interfere with the fixtures used and increase experiment time. Additionally, in the case of three-point bending, irregular specimen ends influenced test results as their irregular geometry can interfere with the test fixture, adding resistance to bending of the specimen.

The generalised steps for specimen preparation are as follows:

1. Using a cutting pliers, cut a section of Cat. A proximal shaft into multiple specimens all of the same length. This length varies between test methods and is specified in Appendix B: Experiment Settings. Take care that the cuts are made at approximately ninety degrees to the length of the shaft axis, as shown in Figure 26.
2. Check the specimen under a digital microscope for defects in the reinforcement and outer layers such as discontinuity of the reinforcement wind, inconsistent pitch, indentation in outer layer material and discoloration of the outer layer material. Examples of inconsistent reinforcement pitch and outer layer defects are shown in Figure 27 and Figure 28 respectively.

3. Inspect both ends of the specimen for protruding reinforcement as shown in Figure 29. If present, remove protruding length with a cutting pliers.
4. Inspect both ends of the specimen for flattening of its cross section as shown in Figure 30. Re-shape by lightly rolling the deformed end between thumb and forefinger if required.

5. Place specimens belonging to the same sample in a bag labelled with the manufacturing date of the specimens, variable between samples and value of that variable.

Once all specimens from all samples are labelled, these specimens are tested with test outputs and specimen tracked through the entire test process. This process was carried out for all testing in the current work.

The methodologies and approaches described in this chapter for test method selection, test method design, experiment design and specimen preparation are used to develop a measurement system capable of measuring a statistically significant difference in mechanical property of Cat. A proximal samples manufactured at high, nominal and low lamination temperatures.
5 Measurement System Development

This chapter describes the test methods developed throughout the duration of this research. A description of the test, justification for its selection and parameters used, test procedure and summary of results obtained. The test method selection methodology is also stated in Section 4.1 Test Method Selection and Design. Full presentation and discussion of experiment results is contained in Chapter 6 Analysis and Discussion and Appendix A: Experiment Data Statistics and Results. In line with the project aim, the results obtained from the test methods investigated are quantitative in nature and presented in the boxplot format shown in Figure 31.

![Boxplot Diagram](image)

*Figure 31 - Format of boxplot used throughout.*

5.1 Kink Diameter Test

The Kink Diameter Test is a test method used in industry for evaluation of kink resistance of catheter devices at the distal, proximal and mid-shaft section. This test method is therefore a natural starting point for testing of proximal shafts made using high, nominal and low lamination temperatures. The result obtained from the test method is the minimum diameter loop the catheter shaft can be held in before kinking occurs. A test specimen of approximately 40 cm is used to allow positioning of the test specimen into the fixture as seen in Figure 33. This entails inserting the specimen through two RHV’s and tightening them to fix the length of specimen between them. The shaft is configured...
into a loop and held this way by a loop insert (shown in Figure 32) with a transparent plate over it.

![Loop insert used on kink diameter test fixture.](image1)

With the test specimen in this starting position, the experimental procedure continues as follows:

1. Record loop measurement using a digital microscope.
2. Turn both micrometres through 360° (corresponding with a linear displacement of 1 mm outward on both sides) and record the loop measurement using the digital microscope.
3. Repeat step 2 until the specimen kinks.

![Kink diameter test arrangement.](image2)
5.1.1 Functionality Experiment

A functionality experiment was carried out using a sample size equal to 6. This was the maximum sample size available due to the time and materials availability constraints associated with an approximate specimen length of 40 cm. No statistically significant difference between high, nominal and low lamination temperature sample groups was measured. The results are shown in Figure 34 and it can be seen that the means of each sample group are similar by their position relative to each other on the vertical axis. The nominal sample data has less variation in comparison to the low and high sample groups for reasons not identified.

![Boxplot of results from kink diameter functionality experiment.](image)

Issues associated with application of this test method on Cat. A proximal shaft specimens were identified from this experiment. Firstly, in order to load the test specimen into the loop insert, it is necessary to plastically deform it. This uncontrolled deformation undoubtedly affects the results from the test in a way difficult to quantify. Secondly, how results are acquired using a digital microscope is also time consuming, sub-optimal and subjective. The large standard deviation of data in each sample is likely caused by this uncontrolled deformation and subjectivity. From the power curve calculation, in order to achieve a statistical power of 0.8, the sample size must be increased to 180 specimens which would prove an extremely time consuming and costly endeavour.
As previously stated, the choice of the kink diameter test as a starting point was because of its current use in industry. However, from this functionality experiment, it is clear that there are significant issues with the use of this test for proximal shaft samples which have a higher bending stiffness. For this reason, it is necessary to consider the application of common materials test methods on Cat. A proximal shaft specimens. Some such test methods are tensile and axial loading tests. Both test methods would significantly improve on the kink diameter test as they require negligible deformation of the test specimen before commencement of the test and use materials testing frame with automated data acquisition. The tensile test is first investigated due to its repeatability, use across many industries and current use in the biomedical industry with ISO 10555.

5.2 Tensile Test

Tensile testing is a fundamental test in materials science and engineering. A test specimen is gripped and pulled in a controlled manner until a pre-defined measurement event such as plastic deformation or breaking occurs. A material’s elastic modulus can be determined using a tensile test and this property is used extensively in mechanics of materials theory for describing the behaviour of materials and structures under load. Requirements for tensile strength of intravascular catheters at each cross section, tubular junction and junction between shaft and hub are described in ISO 10555 [3]. Although a tensile test does not approximate the loading conditions under which the Cat. A proximal shaft is fracturing, use of this method in ISO 10555 indicates that the industry is accepts this. Adapting this standard to measure a mechanical property of the Cat. A proximal shaft may produce results that satisfy the project aim. This is because of the significant increases in sensitivity and repeatability associated with using a materials testing frame.

Adapting the ISO 10555 standard for use on the Cat. A proximal shaft is not without difficulty. No method of gripping the test specimen is defined in the standard so three different grip types are assessed in the functionality experiment. Additionally, the test specimens defined in ISO 10555 are of non-constant cross section so therefore include a point at which stress concentrations can form and induce failure. The Cat. A proximal shaft is of constant cross section so failure is likely to occur where the specimen is gripped due to the stress concentration at that location. This is an issue as to draw meaningful results from tensile test data, the test specimens should break at approximately half the
gauge length. This indicates that the test set-up is not influencing the stress distribution at the break point in the test specimen. To mitigate this issue, a PTFE internal beading is used to reduce the stress concentration at the grips and the tensile test arrangements explored in the functionality experiment are assessed on this criterion.

5.2.1 Functionality Experiment

A functionality experiment is carried out to explore solutions for adapting the tensile test method described in ISO 10555 for use on the Cat. A proximal shaft. The appropriateness of three tensile test arrangements (shown in Figure 35) were assessed by the frequency of breaking at approximately half the gauge length. The displacement rate, specimen length and location of internal support was varied between tests to identify their effect on break location. PTFE rod was used as an internal support during testing to prevent the collapse of the catheter ID when being gripped as shown in Figure 36.

Figure 35 - Tensile test arrangement from left to right: mechanical grips, chord and yarn grips and pneumatic grips with grip covers.
The mechanical grip arrangement was used with the Instron 3345 materials test frame. A 1 kN (2519-1KN) load cell was used due to the weight of the grips which overloaded the 100 N (2519-100) load cell [65]. This corresponded with a decrease in load reading accuracy from 0.2 N to 2 N but as the purpose of this experiment is to establish if break location can be controlled, it was deemed acceptable. Significant issues became apparent with vertical alignment of the test specimen and with inconsistent break location. Misaligned or diagonally held test specimens will be subject to bending loads causing variation in results. Breaking consistently occurred at the grip due to the stress concentration caused by the small contact area and high grip force. This is undesirable as the readings from the test are being affected by an unknown amount by the grips [66].

To mitigate the issue of breaking at the grips further tensile testing was carried out on an Instron 5564 machine with 100 N (2525-807) load cell with a chord and yarn fixture (shown centre of Figure 35). This fixture is designed to reduce stress concentration at the grips for delicate, thin specimens by increasing the contact area of the grip [67]. PTFE rod was used for internal support, the length and positioning of which was varied between specimens to observe which configurations worked best in relation to break location of the specimen. Breaking of the specimens was observed to occur where the internal support ended within the test specimen as illustrated in Figure 36. This can be explained from when the specimen begins to neck, it contacts the internal support which prevents it from necking further, causes a stress concentration and induces failure at that point. This effect was reduced by tapering the internal support to increase the contact area and
therefore reduce the stress concentration but the problem persisted. Additional issues with this test arrangement included the chord and yarn fixture itself. The radius to which the test specimen must be bent in order to load the test specimen into the fixture causes the specimen to plastically yield in an uncontrollable manner. This issue was also observed and discussed in section 5.1 Kink Diameter Test.

The final tensile test arrangement investigated made use of pneumatic grips with 3D printed grip covers to aid in the vertical alignment of the test specimen. These covers can be seen in Figure 35 (right) with a more detailed view in Figure 37. Despite use of the grip covers, the observed issues reflected those seen from testing using the just mechanical grips as breaking continues to occur at the grip.

![Image of catheter specimen held here and pneumatic grip covers fit in this recess](image)

*Figure 37 - Pneumatic grip covers used in the third tensile test arrangement.*

The overall outcome of the functionality experiment was that the tensile test arrangements were deemed inappropriate for use on *Cat. A* proximal shaft specimen. No significant results were obtained in relation to the project aim and for this reason, results of tensile testing are omitted from 6 Analysis and Discussion and Appendix A: Experiment Data Statistics and Results. The benefits of using a materials testing frame remain. A axial loading test method uses a materials test frame and does not require modification to ensure consistent breaking at approximately half of the specimen gauge length. Development of a axial loading test is explored next.
5.3 Axial Loading Test

Axial loading tests are another fundamental form of materials testing. The axial loading test described in this section refers to a test in which the specimens are held in a pinned-pinned configuration and compressed at constant rate of displacement until kinking occurs. The loading conditions introduced by this configuration are like those seen during the manually performed test methods and from insertion of the device into a patient during which failure occurs. The extensive use of axial loading tests in materials testing and the wealth of knowledge that exists on this test configuration also support its choice. A prototype and optimised axial loading test arrangement as shown in Figure 38 were developed with valuable results produced. Experiment settings are included in Appendix B: Experiment Settings.

![Figure 38 - Prototype axial loading test fixture before test (left) at end of test (centre) and optimised compression fixture during test (right).](image)

The measured values chosen for statistical analysis are maximum force (N) and force at break (N). It is the force at break results that are presented for the axial loading test method as they displayed less variability. Testing was carried out using an Instron 3345 materials testing frame with a 100 N (2519-103) series load cell accurate to ± 0.2 N [65, 68].

5.3.1 Functionality Experiment

Initial testing was carried out using a prototype fixture with a functionality experiment carried out. Three sample groups consisting of specimens made from the proximal shafts of different catheter devices are tested. Specimens were prepared from segments of Cat. A proximal shaft as well as two other device’s belonging to the same product family Cat. B
and Cat. C. The proximal shaft of Cat. B and Cat. C catheters are known to have good resistance to kinking whereas Cat. A is not and is also known to fail by fracturing as discussed in Section 1 Introduction.

A sample size of 10 was used which resulted in a statistical power larger than 0.8. Testing of these specimens alongside each other provides a visual comparison of what good kink resistance looks like on a force/displacement graph. This is valuable, new knowledge that may be used to assess the effect of process and design changes on a catheter shaft’s resistance to kinking. Figure 39 is a graph of the force versus displacement for the three samples. The Cat. B and Cat. C products are observed to withstand much larger displacements before kinking than Cat. A. They also exert less resistance to deformation as read from the vertical axis showing Newtons. This suggests that their bending stiffness is less than the Cat. A product which can be explained by the difference in elastic modulus and geometry of the structure [69]. The force displacement graph generated from the raw data can be seen in Figure A3, Appendix A: Experiment Data Statistics and Results. The force readings for the functionality experiment fall to the lower end of the load cells capacity. However, the load cell is accurate across its full range to 0.2 N [65].

![Figure 39 - Representation of average force/displacement curve for each sample based on experiment data. The point at which kink occurs is indicated approximately by a black circle.](image)

Statistical analysis of the force at kink results obtained from this test is shown in Figure 40. The variability of the Cat. A sample is greater than Cat. B and Cat. C samples with no specific cause for this being identified. A statistically significant difference between all three samples was measured which gave reason to carry out further development of this test method on an optimised test configuration.
5.3.2 Determination of Sequence of Events Proceeding Kink

An investigation into the sequence of events proceeding failure of the Cat. A proximal shaft by kink may provide results that can rationalise test method selection for greater sensitivity. This investigation was carried out upon completion of the compression functionality experiment by means of visual inspection using a digital microscope and micro-computed tomography (micro-CT). This investigation also made use of the optimised axial loading test fixture shown in Figure 41. This fixture minimised noise caused by friction at the pinned ends using ball bearings and also improved the dimensions at the pinned ends of the test specimen such that they were aligned more precisely with the axis of rotation of the pin (Appendix G: 3D Printed Fixture Drawings).

Figure 41 - Optimised axial loading test fixture.
Three specimens were imaged: a control, a specimen tested to maximum force and a specimen tested to kink. The point of maximum force and the point associated with failure from kinking of the device are indicated in Figure 42.

Figure 42 - Representation of the force/displacement curve obtained for each specimen from the axial loading experiments

Figure 43 shows a labelled, cross-sectional view of the control specimen as generated using micro-CT imaging. As this image is of a control specimen, it is used to identify areas of delamination and plastic deformation in proceeding micro-CT images in this section. Streaking is present in the micro-CT images as labelled in Figure 43. This is due to an affect called beam hardening and appears between two dense objects (the nitinol reinforcement layer in this case) as dark bands [70] [71].

Figure 43 - Cross-sectional view of the control specimen.
Now considering the specimen tested to maximum force and the specimen tested to kink. Plastic deformation is apparent on the outer layer of both these specimens in the form of stretch marks. The stretch marks appear between the reinforcement layer winds due to adhesion of the outer layer to the reinforcement layer beneath as shown in Figure 44. The effects of this plastic deformation are apparent in the specimen tested to the point of maximum force as it did not return to its initially straight shape when removed from the axial loading test fixture. Inspection of this specimen using micro-CT did not show signs of delamination. It is possible that delamination has begun at this stage but is not visible from micro-CT as any gap between layers that could have formed during the test has been closed due to the elasticity of the reinforcement layer which returns the specimen close to its initial shape.

Figure 44 - Stretch marks in outer layer of specimen tested to maximum force. The bright stripes in the specimen correspond with the location of the reinforcement layer.

As expected, inspection of the specimen tested to failure from kink using digital microscope shows significant deformation of the entire catheter structure. This deformation along with the planes in which the micro-CT images were taken are shown in Figure 45.

Figure 45 - Cat. A specimen tested to kink.
Micro-CT images of this specimen showed significant delamination of the inner and outer layers and plastic deformation of the reinforcement layer as shown in Figure 46. Plastic deformation of the reinforcement layer is also shown in images generated using data from the micro-CT scans in Figure 47. The deformed shape of the reinforcement layer is coincident with the Brazier effect discussed in 3.6 Kinking of Thin Walled Tubes which states that when an initially straight tube is bent uniformly, the longitudinal tension and compression which resist the applied bending moment have in-plane stress components which tends to ovalise the cross-section [37].
The outcome of this investigation yields an insight into the events occurring within the *Cat. A* proximal shaft before failure by buckling: Initially, the polymer elements of the *Cat. A* specimen provides greatest resistance to bending. Once these elements yield and plastically deform, resistance to bending steadily reduces as the deformation increases putting an increased load on the reinforcement layer until that too fails. Identification of the events occurring within a catheter structure during a kink or bend test allows catheter designs to be assessed against one another with insight into the type of design changes needed to achieve device performance characteristics under load. This is valuable knowledge for the design stage of a catheter. However, application of these results in order to achieve a more sensitive test method remains abstract and worthy of further investigation.

5.3.3 Sensitivity Experiment 1

This experiment continues from the Functionality Experiment using the optimised axial loading test fixture. The suitability of this fixture as a process and design effect measurement tool was assessed by testing *Cat. A* specimens made using high, nominal and low lamination temperature processing in line with the project aim. A sample size of 10 was chosen based on specimen availability and as a best guess at what is required for a statistical power of 0.8.

The results from this experiment show that the sample size produced statistical power in excess of 0.8. A statistically significant difference was measured between the low and nominal samples and low and high samples but not between the nominal and high samples as can be interpreted from Figure 48. The low lamination temperature sample has large variability compared to the nominal and high samples the cause of which has not been identified.
5.3.4 Sensitivity Experiment 2

A second experiment was carried out using the optimised axial loading test fixture where the rate of displacement was increased from 2.5 mm/s to the maximum displacement possible of 16 mm/s [68]. The purpose of this experiment was to investigate whether the increase in speed is sufficient to amplify the effects of viscoelasticity in the test specimen. The term “viscoelasticity” describes materials which behave both like an elastic solid and a viscous fluid when undergoing deformation. Elastic materials deform instantaneously when a stress within their elastic region is applied and return to their original state when the stress is removed. A viscous material displays time-dependant behaviour and deforms at a constant rate under constant stress. When the stress is removed the material remains in its deformed state [72]. In some applications, the viscous element of a viscoelastic material is critical as it is this that determines properties such as impact resistance [73]. Impact loads are a type of dynamic load that are applied and removed suddenly and can be produced when a falling object strikes a structure or when two objects collide [23]. It is possible that the viscoelastic properties between samples varies due to the different processing temperatures.

Using the data obtained from sensitivity experiment 1, the required sample size for a statistical power of 0.8 is 5. However, a sample size of 10 specimens is used again to allow a factor of safety for experimental power. This proved adequate in achieving
statistical power of 0.8. The results of this experiment are presented in Figure 49. A statistically significant difference exists between the nominal sample and the high and low samples. This is likely due to noise and variability in the test method itself. The nominal sample has larger variation relative to the low and high samples for reasons not identified.

![Figure 49 - Boxplot of results from axial loading sensitivity experiment 2.](image)

The results obtained from the axial loading test experiments demonstrate insufficient sensitivity and reliability in the test method. The variability between the samples is extreme as can be seen from the boxplots and the relationship between their means is inconsistent. For these reasons, the TPB test configuration is next investigated with rationale for its selection presented in the following section.

### 5.4 Three-Point Bend Test

As described in Sections 3.5.1 Bending and 3.5.2 Buckling, the differential equations for bending moment, shear force and intensity of distributed load at any cross section in an idealised cantilever beam can also be used to describe a structure in buckling. From this theory, a bend test represents the loading conditions under which the Cat. A proximal shaft is failing in the field. The three-point bend test is a common bend test used to
determine the flexural properties of plastics as in ISO 178 “Plastics - Determination of Flexural Properties”. A three-point bend test can also be easily conducted on a materials test frame. The choice of a TPB test configuration after the axial loading test configuration is justified as such.

The suitability of a TPB test for design and process effect evaluation was investigated with informative conclusions in relation to the finalised measurement system being drawn from four experiments. The displacement rate of 0.05 mm/s of the upper anvil was informed by ISO 178 as was the span \( S \) of the supporting anvils which was guided by the following calculation where \( h \) is the specimen height in millimetres [15]:

\[
S = (16 \pm 1)h
\]

\[
S = (16 \pm 1)(2.16)
\]

\[
S = 32.40 \text{ to } 36.72 \text{ mm}
\]

A span of 32 mm was used as this was easily facilitated using the parts that the TPB test fixture is made from.

The measured values chosen for statistical analysis were maximum force (N) and a bending stiffness measurement (N/mm). It is the bending stiffness measurement results that are presented in this and proceeding sections as the difference in mean bending stiffness values for low, nominal and high lamination temperature samples were found to have more significant differences than the maximum force values. Testing was carried out using an Instron 5564 materials testing frame with a 50 N (2525-817) series load cell accurate to \( \pm 0.125 \) N. The fixtures and grips were chosen such that the sum of the force exerted on the load cell by the grips and fixture would not exceed the allowable tare force of 50 N [74].

During testing, the specimen was placed on the supporting anvils of the fixture shown in Figure 50 and centred before a preload of 0.4 - 0.5 N was applied by the loading anvil at a rate of 0.017 mm/s as per ISO 178 [29]. The purpose of this preload was to seat the specimen on the fixture, preventing statistical noise at the start of the test. The specimen is then deflected by the loading anvil until it kinks taking between 5 and 6 mm of
deflection. The specimen length of 45 mm is chosen such that it remains supported throughout the test. Experiment settings are also included in Appendix B: Experiment Settings.

![Image](image.png)

*Figure 50 - Three-point bend test fixture.*

5.4.1 Functionality Experiment

The difference in mechanical properties between units manufactured at high, nominal and low lamination temperature was not significant according to the axial loading test method experiments. For this reason, the functionality experiment using the TPB test arrangement shown in Figure 50 was carried out on three samples with varying reinforcement layer pitch for reasons outlined in Section 4.2 Experimental Design. The reinforcement layer pitch was varied from the nominal value of 304.8 μm to a high value of 406.4 μm and a low value of 203.2 μm. The high and low pitch values differ from the nominal value by 101.6 μm. A sample size of 10 specimens was chosen which produced a statistical power greater than 0.8.

The results of this experiment presented in Figure 51 and shows each sample having a statistically significant difference from the other. The relatively large standard deviation observed in the low pitch setting sample here is caused by variation in the test specimens rather than the method. The small pitch setting used is approaching the tolerance of the winding machine causing more variability in the test specimens. With this variation
explained, the results of the TPB functionality experiment suggest that the test method may be capable of measuring a difference between low, nominal and high lamination temperature specimens.

![Boxplot of results from TPB functionality experiment.](image)

5.4.2 Sensitivity Experiment 1

The sensitivity experiment was carried out in the same way as the functionality experiment. The purpose of this sensitivity experiment is to indicate whether the test arrangement has sufficient sensitivity to detect a known difference between Cat. A proximal shaft specimens manufactured using different lamination temperature settings. A sample size of 10 specimens was chosen in keeping with the functionality experiment.

The results of this testing shown in Figure 52 require further investigative work with the bending stiffness measurement of the low temperature sample having a statistically significant difference with respect to the nominal and high temperature samples. However, computation of the power curve indicated that the statistical power was inadequate. A sample size of 32 is needed for statistical power of 0.8 so the possibility of no difference being measured due to type II error is unacceptably high for this experiment. This provided rationale to carry out further tests with corrected sample size as done in
sensitivity experiment 2. Firstly, the effectiveness of a two-stage TPB test is investigated. This is a test where the specimen undergoes a conditioning stage before testing.

![Boxplot of results from TPB sensitivity experiment 1.](image)

**Figure 52 - Boxplot of results from TPB sensitivity experiment 1.**

5.4.3 Effect of Preconditioning on Device Performance Experiment

Following TPB sensitivity experiment 1, the effectiveness of a two-stage test for accelerating the effects of use on the *Cat. A* proximal shaft was investigated. This type of test draws from fatigue testing principles in which crack propagation is induced from cyclic loading of a test piece [75]. The envisaged effect of pre-conditioning on the *Cat. A* proximal shaft is crack propagation with an increase in fracture occurrence during testing.

The first stage of the test was a pre-conditioning stage in which the test specimen was bent around a diameter 40 mm mandrel by hand four times with the specimen being rotated about its longitudinal axis through ninety degrees after each bend. This stage is shown in Figure 53.
Bending was chosen as this is the primary loading condition under which failure occurs. The diameter of the mandrel was selected such that excessive damage to the test specimen was not incurred allowing the TPB test to be carried out. The number of times the specimen was bent around the mandrel was chosen such that the effects of preconditioning would be approximately uniform throughout the specimen. Specimens had to be straightened by hand after the preconditioning stage as the polymer outer layer had plastically deformed as shown in Figure 54 and some delamination was visible using micro-CT imaging as shown in Figure 55.

Figure 53 - Mandrel used to bend specimen (left) and specimen being bent around mandrel (right) during the preconditioning stage.

Figure 54 - Example of plastic deformation on outer layer of test specimen due to preconditioning process.
The specimens tested were Cat. A proximal shaft specimens manufactured using nominal settings. These specimens were tested until failure using the TPB test arrangement with results indicating that preconditioning had the effect of improving kink resistance and are shown in detail in Appendix A: Experiment Data Statistics and Results. Preconditioned specimens withstood on average 36% more displacement before the point of maximum force and 48% more displacement before kinking compared to the control. The ability of the device to withstand more displacement before kinking is beneficial to the use of the catheter. A physician using a catheter with the same performance as the preconditioned Cat. A device would receive more force feedback before kinking than a non-preconditioned device. This would give the physician greater opportunity to adjust the catheters position and force applied before the device fails.

In terms of the force, the maximum force read from testing of preconditioned specimens was 17% less than the control and the force at kink was 28% less than the control. A statistically significant reduction in bending stiffness measurement between the control and preconditioned specimens was also measured using two sample t-test as shown in Figure 56. This performance reflects that of the Cat. B and Cat. C products tested during the functionality experiment of the axial loading test method. These two products are
known by their manufacturer to have better resistance to kinking and fracturing into two pieces than the *Cat. A* product.

The increase in displacement before kink and reduction in force at kink can be explained by the plastic deformation in the outer layer of the test specimens shown in Figure 54. The areas where the outer layer has plastically deformed will exert less resistance to bending as they have already exceeded their elastic limit. This has the effect of relieving bending stresses in the specimen. The normal use case of the *Cat. A* device would not plastically deform the outer layer in a controlled, gradual manner as is done in the preconditioning stage which is why this effect is not observed in the field.

![Effect of Preconditioning Experiment](image)

*Figure 56 - Boxplot of results from effect of preconditioning experiment.*

The effect of preconditioning was further investigated by the manufacturer using the manual “wrap” test method. The results confirmed that preconditioning of *Cat. A* specimens reduced the occurrence of fracture by 19%. It is hypothesised that delamination of the outer and reinforcement layers (shown in Figure 55) during the preconditioning process reduces the stress at the point where fracture would initiate by allowing movement of the layers. As discussed in Section 2.3 Fractographic Examination, the reinforcement layer otherwise acts as a stress raiser when the catheter is buckled.
When the stress at this point exceeds the strength of the outer layer of the catheter, fracture occurs causing the device to fail catastrophically [8].

The aim of this experiment was to increase the rate of fracture of the device however the results showed a decrease in fracture and an increase in kink resistance. Because of this, preconditioning was not continued for further experiments however these findings are of significant importance to the manufacturer of the Cat. A device. Increase in displacement before kinking and reduction in fracture occurrence are highly desirable design characteristics. Improvements in such characteristics of catheter may result in improvements in procedure time and success rates as well as its selection by a physician instead of a competitor device. Further investigation into the preconditioning process is necessary to benefit from these findings.

5.4.4 Sensitivity Experiment 2

Results in line with the project aim were not produced from the effect of preconditioning on device performance experiment. Therefore, sensitivity experiment 2 follows on from sensitivity experiment 1. Further testing of lamination temperature samples was carried out with its purpose to verify whether the relationship between low, nominal and high samples shown previously from sensitivity experiment 1 is true, an anomaly or caused by insufficient sensitivity (noise) and experimental power. Using the data obtained from sensitivity experiment 1, a sample size calculation was carried out which indicated that a sample size of 32 specimens is needed for a statistical power of 0.8. However, 30 specimens were used due to availability. The resulting data was used for a statistical power calculation which indicated that the required sample size for statistical power of 0.8 is 7. This change in required sample size from 32 to 7 specimens corresponds with a change in the largest difference between means from 0.46 to 0.94 for sensitivity experiments 1 and 2 respectively, the reasons for which are discussed next.

The results from this experiment are shown in Figure 57 and repeat the pattern shown previously in Figure 52 from TPB sensitivity experiment 1. However, as previously stated, the largest difference between means has increased by factor of more than 2. This could be due to statistical noise caused by insufficient sensitivity of the test method or by a variable that was not controlled during manufacture of the specimens which was the machine used in the lamination process. The 232.22 °C lamination temperature (nominal)
sample was manufactured on a laminator machine used for production and the 220.56 °C (low) and 243.89 °C (high) lamination temperature samples manufactured on a laminator machine used to manufacture product for research and development (R&D) purposes. The reason for this is that production laminator machine produces Cat. A at nominal settings to be sold to customers. The R&D laminator machine has manufactured all Cat. A specimens tested in this research (excluding the nominal sample discussed here). In this instance, due to a shortage of research and development material the nominal sample specimens were taken from those which had been made using the production laminator machine.

To investigate if the results were affected significantly by this, the nominal sample was re-made using the R&D laminator machine and tested using the TPB test method. The nominal samples made on both laminator machines were compared using a two-sample t-test with results showing a statistically significant difference measured between the two samples and is presented in Figure 58.

*Figure 57 - Boxplot of results from TPB sensitivity experiment 2.*
Correcting the nominal data presented in Figure 57 such that all the data is measured from specimens made on the R&D lamination machine yields the boxplot presented in Figure 59. The largest difference between means is greatly reduced from 0.94 to 0.52 which is comparable to that from sensitivity experiment 1. This difference between means is discussed again later in Section 5.5.2 Sensitivity Experiment 2. Computing the power curve results in a required sample size of 22 for statistical power of 0.8.
Confounding variables due to manufacture of product on different machines is a common problem seen in design of experiments. Once a confounding variable has been identified, it can be accounted for through strategies such as restriction, randomisation or matching [76]. As the confounding effect of production laminator machine was noticed at the time it was used, implementation of the restriction control method was without difficulty. This is not an ideal solution as manufacturing all the test specimens using the same laminator machine allows potential for bias. Control by randomisation reduces bias but in the case of this research, it is not a practical option due the limited availability of the production laminator machine [76].

5.4.5 Sensitivity Experiment 3

The purpose of this experiment was to repeat sensitivity experiment 2 to see if a reduction in variability could be achieved. As the useable data gathered from sensitivity experiment 2 had required setting up the test fixture twice, additional variability was introduced due to slight changes in alignment of the fixture. The sample size used was 30 specimens to maintain similarity between sensitivity experiment 2 and 3.

The results of this test are presented in Figure 60. The pooled standard deviation reduced to 0.31 compared to 0.54 measured from the usable data obtained from sensitivity experiment 2. This confirms that there is variation in how the test fixture is set-up. This is likely due to alignment issues. However, the results show a different pattern to the results of sensitivity experiment 1 and 2. This shows that the test method is not reliable enough to accurately measure the difference between Cat. A proximal shaft test specimens made at high, nominal and low lamination temperature. The test method is observed to give reliable readings as per the functionality experiment but these results fall over a larger interval with a maximum difference in means of 5.45 N/mm in comparison to 0.46, 0.94 and 0.43 N/mm for sensitivity experiments 1, 2 and 3 respectively.
Determination of the sensitivity of the TPB test could be completed by carrying out additional experiments where pitch is used as the variable but the difference between the high and low sample from the nominal sample decreases incrementally until the relationship between bending stiffness measurement and pitch is no longer appearing reliably. The interval for which the test method can be said to reliably produce data may be taken as the interval in which results show the same expected relationship before becoming noisy.

Another source of error associated with the TPB test arrangement is the coincidence of the point of application of load with the region of failure on the specimen. Overall, several potential improvements to the measurement system have been identified from the TPB test. These are addressed with the FPB test investigated next.

5.5 Four-Point Bend Test

Due to the insufficient sensitivity observed in results from the experiments carried out using the Axial Loading and TPB test arrangements, the FPB test arrangement is next considered for the following reasons: A FPB test eliminates shear at the longitudinal centre of the test specimen where failure occurs and it allows the specimen to fail near pure bending which is more relevant to how the device fails during use [9]. Additionally, FPB is suitable for non-homogenous test specimens as the stress concentration on the specimen is spread between the two loading anvils whereas for a TPB test, it is
concentrated under the single loading anvil which is coincident with the region in which failure occurs [77]. The FPB test arrangement was informed and adapted from the plastics industry using ASTM d6272 “Standard Test for Flexural Properties of Unreinforced and Reinforced Plastics”. In this standard, two support span arrangements are defined as pictured in Figure 61 [78].

ASTM d6272 defines a support span of 16:1 to be used for sheet materials 1.6 mm or greater in thickness, moulding materials and high strength reinforced composites [78]. Taking the thickness of the test specimen as 2.16 mm which is the diameter of the Cat. A proximal shaft, the support span equates to 34.56 mm. This falls in the range of 32.40 to 36.72 mm as called for in ISO 178 which was used to inform the TPB test arrangement [29]. In order to maintain similarity between the TPB and FPB test, a support span of 32 mm was used. It is rationalised by the author that maintaining this similarity is more important than changing the support span to fit test guidelines as the effect of loading anvil type on the specimen could be assessed without the span as a confounding variable. This is important when comparing results of the TPB and FPB tests as a difference in results can be attributed to the loading anvil type. Additionally, the span of 32 mm is less than 1.5% outside of the specified range which was acceptable to the author.

A prototype fixture was designed and fabricated by the author using the same material used for the TPB test fixture with a support span of 32 mm and load span of 10.67 mm conforming with the “one third of support span” configuration shown in Figure 61. Rudimentary testing was carried out to see if the specimen would fail between the two loading anvils as intended but this was not the case. The test specimen was observed to
deform significantly at the loading anvil and between the loading anvil and supporting anvil in a manner not consistent with pure bending and shown in Figure 62.

![Image of deformation](image)

*Figure 62 - Rudimentary FPB test arrangement showing deformation not consistent with pure bending.*

It is observed that a possible cause for this is the large diameter of the loading and supporting anvils which causes the distance between the points of contact of the specimen and loading and support anvils on either side to reduce as the test progresses i.e. the distance between points of contact on either side reduce from 10.67 mm to 3.17 mm (the load span minus the diameter of the loading/supporting anvil). This results in significant stress concentrations under the loading anvils which plastically deform the test specimen as shown in Figure 63.

![Deformed Cat. A specimen](image)

*Figure 63 - Deformed Cat. A specimen after rudimentary FPB test.*

To mitigate these problems, a reduced anvil diameter FPB fixture was designed by the author which is shown in Figure 64. The fixture maintained the “one third of support span” configuration shown in Figure 61. This fixture was designed to be manufactured in polymer using a 3D printing manufacturing process. This process allows standardisation
of the test method throughout a company or industry quicker, cheaper and easier compared to traditional manufacturing methods. Fixtures can be made cheaply on-site by an automated machine with little manufacturing time and no wait time associated with delivery. Testing using this fixture yielded collapse of the test specimen structure under the loading anvil and not between the loading anvils as shown in Figure 65.

![Figure 64 - Reduced anvil diameter FPB fixture.](image)

![Figure 65 - Collapse of Cat. A specimen under the loading anvil during preliminary FPB testing.](image)

It was decided that the design complexity and inherent increase in test duration involved with a fixture designed to displace a catheter specimen until failure by pure bending between the two loading anvils was not practical. As the deflected shape of the specimen remained unaffected by the geometry of the loading anvils at small displacements, an optimised FPB test fixture with reduced anvil radius was designed by the author for small displacement testing as shown in Figure 66 and Figure 67.
Small displacement of the test specimen is sufficient for calculation of the bending stiffness measurement. The initial linear portion of the displacement curve is divided into sections and the slope of each section is calculated. The steepest slope is calculated as elastic modulus or the bending stiffness measurement. Whether elastic modulus or the bending stiffness measurement is calculated is dependent on the test readings input into the algorithm. For elastic modulus, the readings are stress and strain, for the bending stiffness measurement, force and displacement are used [79]. How the algorithm works is described in Instron’s Bluehill software as follows [80]:

- Searches the data between the data point that is equal to 2% of the maximum force value and the maximum force value.
- The data is checked for a point of zero slope.
- If a point of zero slope is present, the data is divided into 6 equal regions between the first data point and the point of zero slope.
- The algorithm determines which region has the highest slope and assigns elastic modulus or bending stiffness measurement to that region.
In addition to its optimisation for small displacement testing, a number of improvements over the TPB test fixture were incorporated into the optimised FPB test fixture design. As identified from the TPB testing, variability was being introduced to experiment results from setting up of the test fixture. To mitigate this, the optimised FPB test fixture is designed to align with the top and one side of the pneumatic grips used on the Instron testing frame. Additionally, grooved geometry is incorporated on the supporting anvils to reduce lateral movement of the test specimen. These features are shown in Figure 67.

![Figure 67 - Features of the support anvil which aid in alignment with the pneumatic grips. These features are also present on the loading anvil.](image)

A tool for aligning the loading and supporting anvils in agreement with the one third support span designation was also designed and is shown in Figure 68. The alignment tool combined with the geometry for aligning the loading and supporting anvils with the pneumatic clamps significantly reduce variability between experiments caused by differences in alignment. Use of this FPB test fixture designed and developed by the author on Cat. A specimens to great effect is discussed in the following sections with experiment settings given in Appendix B: Experiment Settings.
5.5.1 Sensitivity Experiment 1

As this test is similar to the TPB test with respect to supporting anvil span, preload, rate of displacement and measured value taken for statistical analysis, a functionality test was not carried out. A sensitivity experiment is completed using *Cat. A* specimens with reinforcement layer pitch as the variable. These specimens are manufactured using the same settings as the specimens tested in the TPB functionality experiment. This is to provide data that can be directly compared to that reliably obtained using the TPB test method. Lamination temperature is not used as the test variable as results of such testing using the TPB test method was not reliable. The sample size was adjusted to 14 to agree with the power curve calculation carried out using TPB sensitivity experiment 3. The resulting power associated with this experiment exceeds 0.8.

The results obtained from this experiment as shown in Figure 69 have a maximum difference between means of 7.78 N/mm. From the TPB functionality experiment this number is 5.45 N/mm suggesting that the FPB test is capable of measuring differences between test specimens more accurately. These results are promising with each sample having a statistically significant difference from the other. Similar to the results of the TPB functionality experiment, a relatively large standard deviation is observed in the low pitch setting sample due to greater variation in the test specimens rather than the test method.
5.5.2 Sensitivity Experiment 2
The purpose of this experiment is to assess the FPB test set-up with respect to the project aim by testing high, nominal and low lamination temperature samples. This experiment was carried out using the same settings including sample size as FPB Sensitivity 1. The only deviation from FPB sensitivity experiment 1 is the processing of the test specimens.

The results are shown in Figure 70 where a statistically significant difference was measured between all three samples, satisfying the project aim. Relatively equal variances between samples were also measured. The relationship between samples shows a decrease in the bending stiffness of the Cat. A proximal shaft. Further investigation is necessary to determine the cause of this relationship. However, the FPB test appears to have sufficient sensitivity to lend itself to such an investigation.
In conclusion, the results of the FPB sensitivity experiment 2 represent convergence on the project aim using the test method development methodology. Measurement of a statistically significant difference between lamination temperature samples has not been achieved previously. Additionally, increase of the mean interval has increased from 0.52 N/mm obtained from TPB sensitivity experiment 2 (the largest attained using the TPB test method) method to 2.65 N/mm. This illustrates the improvement in test method sensitivity which made possible the detection of very small differences between samples caused by varying energy absorbed by the test specimen during lamination processing. Therefore, in satisfaction of the project aim, the final measurement system should comprise of the FPB test arrangement described in this section. Detailed instructions for apparatus, test set-up, computer programme, procedures and record keeping required for the measurement system are presented in Appendix C: Finalised Measurement System.
6 Analysis and Discussion

This section describes in detail results of interest obtained from the experiments carried out in fulfilment of the project aim. The test methods are reviewed in terms of pooled standard deviation and mean interval of results. Pooled standard deviation is the average spread of all data points about their sample group mean [81]. Larger variability in results indicate issues with repeatability of the test arrangement and/or variability in the test specimens.

The trend of the pooled standard deviation for experiments with lamination temperature as the variable reduces as shown in Figure 71. The data shown was gathered from test specimens manufactured using the same equipment, operator and materials. This reduction in variability is indicative of steady improvement in the measurement system and shows convergence of the measurement system development methodology on a solution that fulfils the project aim. The complete measuring system is defined in Appendix C: Finalised Measurement System.

![Figure 71 - Individual value plot of pooled SD of experiments with lamination temperature as variable.](image-url)
The largest variability is observed in results from the kink diameter functionality experiment. This variability is explained by pitfalls in the test procedure such as the unavoidable damage during loading of the test specimen into a loop configuration. Measurement of the experiment results using a digital microscope is also subjective. Both of these issues were addressed with subsequent compression, TPB and FPB test arrangements. Deformation of the test specimen before carrying out the test was no longer needed as the specimen could be placed in or onto the fixture in its initially straight shape. Data acquisition was carried out digitally using built in transducers and data acquisition device’s associated with the Instron 3345 and 5564 test machines, removing subjectivity.

The mean interval for experiments with lamination temperature as the variable increased as shown in Figure 72. The interval over which results fall can be used as an indicator for the effective resolution of the measurement system. As the input remains constant, a larger mean interval indicates that the measurement system can detect a smaller input [82]. The largest mean interval is observed from FPB sensitivity experiment 2 which uses the test arrangement recommended for the final measurement system. Additionally, various alignment aids were incorporated into the design of the FPB test fixture as discussed in Section 5.5.2.

![Individual Value Plot](image.png)

*Figure 72 - Individual value plot of mean interval of experiments with lamination temperature as variable.*
The reduction in pooled standard deviation and mean interval in addition to the detection of a statistically significant difference between three sample groups made at high, nominal and low lamination temperature settings, using the FPB also highlights how sensitive the Cat. A specimens are to point loading. This was previously believed to be of negligible effect however, the performance of the FPB test compared to the TPB test supports the claim that coincidence of the point of failure with the point of application of load is detrimental to the effective resolution of the measurement system. A complete measuring system satisfying the project aim is presented in Appendix C: Finalised Measurement System.

The outcomes of this research represent a significant contribution to neurovascular catheter design and to the field of intravenous medicine. The resulting measurement system is the first of its kind to demonstrate great enough sensitivity to detect a difference in mechanical property of the Cat. A proximal shaft manufactured at different lamination temperatures. Use of this measurement system in the place of the existing manual test methods will accelerate the development of future products as well as investigations into failures of existing product through increase in repeatability and output of quantitative results. Findings in relation to preconditioning of the Cat. A proximal shaft before TPB testing, show dramatic increase in kink and fracture resistance. Development of the preconditioning stage into a validated manufacturing process would improve the catheter performance with strong positive implications for the field of intravenous medicine. Conclusions from this research are presented in the following final chapter.

The effect of preconditioning was further investigated by the manufacturer using the manual “wrap” test method. The results confirmed that preconditioning of Cat. A specimens reduced the occurrence of fracture by 19%. It is hypothesised that delamination of the outer and reinforcement layers (shown in Figure 55) during the preconditioning process reduces the stress at the point where fracture would initiate by allowing movement of the layers. As discussed in Section 2.3 Fractographic Examination, the reinforcement layer otherwise acts as a stress raiser when the catheter is buckled. When the stress at this point exceeds the strength of the outer layer of the catheter, fracture occurs causing the device to fail catastrophically.
7 Conclusions

The aim of this research was to develop a measurement system that can produce quantitative results for evaluating process and design changes in the proximal shaft of Cat. A. The resulting instruments, operations, methods, fixtures and software described in Section Appendix C: Finalised Measurement System is practical, repeatable, reliable and sensitive enough to fulfil this aim.

Three sample groups were tested per a measurement system development plan using a number of test methods. Each test method was changed from the previously used system with the objective of increasing sensitivity. A 72 % reduction in the pooled standard deviation of results between the first and last test was achieved. The test method development plan was also very successful at drastically increasing sensitivity and resolution with a 482 % increase in mean interval of experiment results from the first and last measurement systems. These figures are testament to the effectiveness of the test method development plan with addressing issues with repeatability and sensitivity. These vast improvements were achieved through literature review, development of appropriate statistical methods and methodical selection and development of various test arrangements.

The culmination of the work contained in this thesis is the invention of the FPB test measurement system. Implementation of this measurement system in the design process for future catheter designs and in the investigation of the causes of fracture in the Cat. A proximal shaft is fully justified using the enclosed and referenced works. Test fixture, programme and SOP are defined to minimise the effort and cost needed by the industrial sponsor to standardise this test method internally.

In conclusion, the methodology used for test method development has been successful in developing a measurement system to replace the existing non-standardised, manual test methods. This measurement system produces quantitative results with a sensitivity great enough to evaluate the effect of minor process and design changes on the Cat. A proximal shaft. Avenues worthy of further research have also been identified.
References


Appendix A: Experiment Data Statistics and Results

Kink Diameter Functionality Experiment

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count N</th>
<th>N*</th>
<th>Q1 Median</th>
<th>Q3 Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>6</td>
<td>6</td>
<td>0 18.367 19.813 21.409</td>
<td>4.870 3.041</td>
<td></td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>6</td>
<td>6</td>
<td>0 18.318 19.300 19.874</td>
<td>2.996 1.556</td>
<td></td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>6</td>
<td>6</td>
<td>0 17.221 19.622 20.822</td>
<td>5.395 3.601</td>
<td></td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal
Alternative hypothesis: Not all means are equal
Significance level: $\alpha = 0.05$

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>0.9187</td>
<td>0.4593</td>
<td>0.16</td>
<td>0.853</td>
</tr>
<tr>
<td>Within</td>
<td>15</td>
<td>42.7271</td>
<td>2.8485</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>43.6457</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>6</td>
<td>19.698</td>
<td>1.845</td>
<td>(18.229, 21.166)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>6</td>
<td>19.144</td>
<td>1.015</td>
<td>(17.676, 20.613)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>6</td>
<td>19.415</td>
<td>2.027</td>
<td>(17.947, 20.884)</td>
</tr>
</tbody>
</table>

Pooled SD = 1.68774

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>6</td>
<td>19.698 A</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>6</td>
<td>19.415 A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>6</td>
<td>19.144 A</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.
Power Curve Calculation

One-way ANOVA
\[ \alpha = 0.05 \quad SD_p = 1.68774 \]
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.554</td>
<td>180</td>
<td>0.8</td>
<td>0.800376</td>
</tr>
</tbody>
</table>

The sample size is for each level.

![Power Curve for One-way ANOVA](image)

Figure A1 - Power curve for kink diameter functionality experiment

Axial Loading Functionality Experiment

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. A</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>2.0441</td>
<td>2.1918</td>
<td>2.4876</td>
<td>0.6604</td>
<td>0.4435</td>
</tr>
<tr>
<td>Cat. B</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>1.7654</td>
<td>1.7978</td>
<td>1.8302</td>
<td>0.1287</td>
<td>0.0649</td>
</tr>
<tr>
<td>Cat. C</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>1.1882</td>
<td>1.2327</td>
<td>1.2452</td>
<td>0.1801</td>
<td>0.0570</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis  All means are equal
Alternative hypothesis  Not all means are equal
Significance level  \[ \alpha = 0.05 \]

Equal variances were assumed for the analysis.
Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3</td>
<td>Cat. A, Cat. B, Cat. C</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>5.4458</td>
<td>2.72291</td>
<td>121.55</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>27</td>
<td>0.6048</td>
<td>0.02240</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>6.0507</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. A</td>
<td>10</td>
<td>2.2652</td>
<td>0.2515</td>
<td>(2.1681, 2.3624)</td>
</tr>
<tr>
<td>Cat. B</td>
<td>10</td>
<td>1.7953</td>
<td>0.0402</td>
<td>(1.6982, 1.8924)</td>
</tr>
<tr>
<td>Cat. C</td>
<td>10</td>
<td>1.2233</td>
<td>0.0486</td>
<td>(1.1262, 1.3204)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.149672

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. A</td>
<td>10</td>
<td>2.2652</td>
<td>A</td>
</tr>
<tr>
<td>Cat. B</td>
<td>10</td>
<td>1.7953</td>
<td>B</td>
</tr>
<tr>
<td>Cat. C</td>
<td>10</td>
<td>1.2233</td>
<td>C</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA

α = 0.05  SDp = 0.149672
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0419</td>
<td>2</td>
<td>0.8</td>
<td>0.928407</td>
</tr>
</tbody>
</table>

The sample size is for each level.
Axial Loading Sensitivity Experiment 1

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>9</td>
<td>1</td>
<td>6.713</td>
<td>6.993</td>
<td>8.249</td>
<td>2.895</td>
<td>1.536</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>9</td>
<td>1</td>
<td>5.900</td>
<td>5.987</td>
<td>6.849</td>
<td>1.585</td>
<td>0.948</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>5.357</td>
<td>5.855</td>
<td>5.964</td>
<td>0.947</td>
<td>0.607</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal
Alternative hypothesis: Not all means are equal
Significance level: $\alpha = 0.05$
Rows unused: 2

Equal variances were assumed for the analysis.
Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>12.26</td>
<td>6.1288</td>
<td>14.21</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>25</td>
<td>10.78</td>
<td>0.4313</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>23.04</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>9</td>
<td>7.331</td>
<td>0.950</td>
<td>(6.880, 7.782)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>9</td>
<td>6.248</td>
<td>0.568</td>
<td>(5.797, 6.699)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>5.747</td>
<td>0.331</td>
<td>(5.320, 6.175)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.656762

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>9</td>
<td>7.331</td>
<td>A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>9</td>
<td>6.248</td>
<td>B</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>5.747</td>
<td>B</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA

α = 0.05 \( SD_p = 0.6567 \)

Factors: 1 Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.584</td>
<td>5</td>
<td>0.8</td>
<td>0.858766</td>
</tr>
</tbody>
</table>

The sample size is for each level.
Figure A4 - Power curve for axial loading sensitivity experiment 1.

Axial Loading Sensitivity Experiment 2

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>4.829</td>
<td>4.990</td>
<td>5.422</td>
<td>1.384</td>
<td>0.593</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>5.273</td>
<td>6.812</td>
<td>8.330</td>
<td>5.549</td>
<td>3.057</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>9</td>
<td>1</td>
<td>4.648</td>
<td>4.997</td>
<td>5.551</td>
<td>1.861</td>
<td>0.902</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal
Alternative hypothesis: Not all means are equal
Significance level: \( \alpha = 0.05 \)

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3</td>
<td>220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>17.53</td>
<td>8.764</td>
<td>7.27</td>
<td>0.003</td>
</tr>
<tr>
<td>Within</td>
<td>26</td>
<td>31.36</td>
<td>1.206</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>48.89</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>5.115</td>
<td>0.427</td>
<td>(4.401, 5.829)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>6.748</td>
<td>1.731</td>
<td>(6.034, 7.462)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>9</td>
<td>5.110</td>
<td>0.587</td>
<td>(4.357, 5.862)</td>
</tr>
</tbody>
</table>

Pooled SD = 1.09823

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>6.748</td>
<td>A</td>
</tr>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>5.115</td>
<td>B</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>9</td>
<td>5.110</td>
<td>B</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \)  \( \text{SD}_{p} = 1.09823 \)
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.638</td>
<td>10</td>
<td>0.8</td>
<td>0.812642</td>
</tr>
</tbody>
</table>

The sample size is for each level.

Figure A5 - Power curve for axial loading sensitivity experiment 2.
TPB Functionality Experiment

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>16.804</td>
<td>18.041</td>
<td>18.923</td>
<td>3.393</td>
<td>2.119</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>14.554</td>
<td>14.666</td>
<td>15.134</td>
<td>0.867</td>
<td>0.580</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>12.216</td>
<td>12.621</td>
<td>12.860</td>
<td>1.320</td>
<td>0.643</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal  
Alternative hypothesis: Not all means are equal  
Significance level: $\alpha = 0.05$

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 203.2 μm pitch, 304.8 μm pitch, 406.4 μm pitch</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>140.38</td>
<td>70.1919</td>
<td>134.34</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>27</td>
<td>14.11</td>
<td>0.5225</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>154.49</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>10</td>
<td>17.856</td>
<td>1.140</td>
<td>(17.387, 18.325)</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>10</td>
<td>14.8043</td>
<td>0.3136</td>
<td>(14.3353, 15.2733)</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>10</td>
<td>12.578</td>
<td>0.412</td>
<td>(12.109, 13.047)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.722848

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>10</td>
<td>17.856</td>
<td>A</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>10</td>
<td>14.8043</td>
<td>B</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>10</td>
<td>12.578</td>
<td>C</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.
Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \)  
\( SD_p = 0.722848 \)
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.278</td>
<td>2</td>
<td>0.8</td>
<td>0.946630</td>
</tr>
</tbody>
</table>

The sample size is for each level.

Figure A6 - Power curve for TPB functionality experiment.

TPB Sensitivity Experiment 1

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Mean</th>
<th>StDev</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>13.086</td>
<td>0.766</td>
<td>12.525</td>
<td>13.162</td>
<td>13.696</td>
<td>2.384</td>
<td>1.171</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>13.501</td>
<td>0.585</td>
<td>13.167</td>
<td>13.532</td>
<td>13.872</td>
<td>2.115</td>
<td>0.705</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>13.545</td>
<td>0.261</td>
<td>13.385</td>
<td>13.448</td>
<td>13.716</td>
<td>0.860</td>
<td>0.330</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis       All means are equal
Alternative hypothesis Not all means are equal
Significance level    \( \alpha = 0.05 \)

Equal variances were assumed for the analysis.
Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3</td>
<td>220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>1.284</td>
<td>0.6420</td>
<td>1.93</td>
<td>0.165</td>
</tr>
<tr>
<td>Within</td>
<td>27</td>
<td>8.982</td>
<td>0.3327</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>10.266</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>13.086</td>
<td>0.766</td>
<td>(12.712, 13.460)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>13.501</td>
<td>0.585</td>
<td>(13.127, 13.875)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>13.540</td>
<td>0.2614</td>
<td>(13.1707, 13.9192)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.576783

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>243.89 °C lam. temp.</td>
<td>10</td>
<td>13.540</td>
<td>A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>10</td>
<td>13.501</td>
<td>A</td>
</tr>
<tr>
<td>220.56 °C lam. temp.</td>
<td>10</td>
<td>13.086</td>
<td>A</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA

| α = 0.05 | SD_p = 0.576783 |
| Factors: 1 | Number of levels: 3 |

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.459</td>
<td>32</td>
<td>0.8</td>
<td>0.807511</td>
</tr>
</tbody>
</table>

The sample size is for each level.
TPB Sensitivity Experiment 2

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>13.266</td>
<td>13.670</td>
<td>14.462</td>
<td>3.095</td>
<td>1.197</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>14.529</td>
<td>14.736</td>
<td>14.941</td>
<td>2.787</td>
<td>0.412</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>13.942</td>
<td>14.223</td>
<td>14.586</td>
<td>1.408</td>
<td>0.644</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal
Alternative hypothesis: Not all means are equal
Significance level: $\alpha = 0.05$

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>13.14</td>
<td>6.5696</td>
<td>25.96</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>86</td>
<td>21.77</td>
<td>0.2531</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>88</td>
<td>34.91</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>13.814</td>
<td>0.713</td>
<td>(13.631, 13.996)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>29</td>
<td>14.7574</td>
<td>0.2785</td>
<td>(14.5716, 14.9431)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.2989</td>
<td>0.4089</td>
<td>(14.1163, 14.4815)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.503091

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>232.22 °C lam. temp.</td>
<td>29</td>
<td>14.7574</td>
<td>A</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.2989</td>
<td>B</td>
</tr>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>13.814</td>
<td>C</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA

\( \alpha = 0.05 \), \( \text{SDP} = 0.503091 \)

Factors: 1, Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9434</td>
<td>7</td>
<td>0.8</td>
<td>0.829838</td>
</tr>
</tbody>
</table>

The sample size is for each level.

![Power Curve for One-way ANOVA](image)

*Figure A8 - Power curve for TPB sensitivity experiment 2.*
Effect of Preconditioning on Device Performance Experiment

Two Sample T-Test for Max Force

Two Sample T-Test Method

\( \mu_1 \): mean of Max Force when C2 = Control
\( \mu_2 \): mean of Max Force when C2 = Pre-Conditioned

Difference: \( \mu_1 - \mu_2 \)

*Equal variances are assumed for this analysis.*

Descriptive Statistics: Max Force

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>1.970</td>
<td>0.103</td>
<td>0.033</td>
</tr>
<tr>
<td>Pre-Conditioned</td>
<td>10</td>
<td>1.6312</td>
<td>0.0859</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Estimation for Difference

<table>
<thead>
<tr>
<th>Difference</th>
<th>SD_p</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3384</td>
<td>0.0950</td>
<td>(0.2491, 0.4276)</td>
</tr>
</tbody>
</table>

Test

Null hypothesis \( H_0: \mu_1 - \mu_2 = 0 \)
Alternative hypothesis \( H_A: \mu_1 - \mu_2 \neq 0 \)

<table>
<thead>
<tr>
<th>T-Value</th>
<th>DF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.97</td>
<td>18</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Figure A9 - Boxplot of max force result from effect of preconditioning experiment.*
Two Sample T-Test for Disp. At Kink

Two Sample T-Test Method

\[ \mu_1: \text{mean of Disp. at Break when } C2 = \text{Control} \]
\[ \mu_2: \text{mean of Disp. at Break when } C2 = \text{Pre-Conditioned} \]

Difference: \( \mu_1 - \mu_2 \)

Equal variances are assumed for this analysis.

Descriptive Statistics: Disp. at Kink

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>11.85</td>
<td>0.65</td>
<td>0.21</td>
</tr>
<tr>
<td>Pre-Conditioned</td>
<td>10</td>
<td>17.48</td>
<td>5.76</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Estimation for Difference

<table>
<thead>
<tr>
<th>Difference</th>
<th>SD_p</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5.63</td>
<td>4.10</td>
<td>(-9.48, -1.78)</td>
</tr>
</tbody>
</table>

Test

Null hypothesis \( H_0: \mu_1 - \mu_2 = 0 \)
Alternative hypothesis \( H_1: \mu_1 - \mu_2 \neq 0 \)

\( T \)-Value \( DF \) \( P \)-Value
\(-3.07\) \( 18 \) \( 0.007 \)

![Boxplot of disp. at kink result from effect of preconditioning experiment.](image)

Two Sample T-Test for Force at Kink

Two Sample T-Test Method
\( \mu_1 \): mean of Force at Break when \( C_2 = \text{Control} \)

\( \mu_2 \): mean of Force at Break when \( C_2 = \text{Pre-Conditioned} \)

Difference: \( \mu_1 - \mu_2 \)

Equal variances are assumed for this analysis.

**Descriptive Statistics: Force at Kink**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>1.5314</td>
<td>0.0849</td>
<td>0.027</td>
</tr>
<tr>
<td>Pre-Conditioned</td>
<td>10</td>
<td>1.099</td>
<td>0.348</td>
<td>0.11</td>
</tr>
</tbody>
</table>

**Estimation for Difference**

<table>
<thead>
<tr>
<th>Difference</th>
<th>SDp</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.432</td>
<td>0.253</td>
<td>(0.195, 0.670)</td>
</tr>
</tbody>
</table>

**Test**

Null hypothesis: \( H_0: \mu_1 - \mu_2 = 0 \)

Alternative hypothesis: \( H_1: \mu_1 - \mu_2 \neq 0 \)

<table>
<thead>
<tr>
<th>T-Value</th>
<th>DF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.82</td>
<td>18</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Figure A11 - Boxplot of force at kink result from effect of preconditioning experiment.*
Two Sample T-Test for Displacement at Max Force

Two Sample T-Test Method

μ₁: mean of Disp. at Max Force when C2 = Control
μ₂: mean of Disp. at Max Force when C2 = Pre-Conditioned
Difference: μ₁ - μ₂

Equal variances are assumed for this analysis.

Descriptive Statistics: Disp. at Max Force

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>6.446</td>
<td>0.191</td>
<td>0.061</td>
</tr>
<tr>
<td>Pre-Conditioned</td>
<td>10</td>
<td>8.755</td>
<td>0.760</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Estimation for Difference

<table>
<thead>
<tr>
<th>Difference</th>
<th>SDp</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2.309</td>
<td>0.554</td>
<td>(-2.830, -1.788)</td>
</tr>
</tbody>
</table>

Test

Null hypothesis H₀: μ₁ - μ₂ = 0
Alternative hypothesis H₁: μ₁ - μ₂ ≠ 0

<table>
<thead>
<tr>
<th>T-Value</th>
<th>DF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-9.32</td>
<td>18</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Figure A12 - Boxplot of disp. at max force result from effect of preconditioning experiment.
Two Sample T-Test for Bending Stiffness Measurement

Two Sample T-Test Method

\( \mu_1 \): mean of Control
\( \mu_2 \): mean of Pre-Conditioned
Difference: \( \mu_1 - \mu_2 \)

Equal variances are assumed for this analysis.

Descriptive Statistics

<table>
<thead>
<tr>
<th>Sample</th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>4.496</td>
<td>0.189</td>
<td>0.060</td>
</tr>
<tr>
<td>Pre-Conditioned</td>
<td>10</td>
<td>2.978</td>
<td>0.284</td>
<td>0.090</td>
</tr>
</tbody>
</table>

Estimation for Difference

<table>
<thead>
<tr>
<th>Difference</th>
<th>SD_p</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.518</td>
<td>0.241</td>
<td>(1.291, 1.745)</td>
</tr>
</tbody>
</table>

Test

Null hypothesis \( H_0: \mu_1 - \mu_2 = 0 \)
Alternative hypothesis \( H_1: \mu_1 - \mu_2 \neq 0 \)

<table>
<thead>
<tr>
<th>T-Value</th>
<th>DF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.06</td>
<td>18</td>
<td>0.000</td>
</tr>
</tbody>
</table>
TPB Sensitivity Experiment 2 with Corrected Data

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>13.266</td>
<td>13.670</td>
<td>14.462</td>
<td>3.095</td>
<td>1.197</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>13.944</td>
<td>14.283</td>
<td>14.722</td>
<td>1.848</td>
<td>0.778</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>13.942</td>
<td>14.223</td>
<td>14.586</td>
<td>1.408</td>
<td>0.644</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis: All means are equal
Alternative hypothesis: Not all means are equal
Significance level: α = 0.05

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3</td>
<td>220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>5.110</td>
<td>2.5548</td>
<td>8.63</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>87</td>
<td>25.754</td>
<td>0.2960</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td>30.863</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>13.814</td>
<td>0.713 (13.616, 14.011)</td>
<td></td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>30</td>
<td>14.3373</td>
<td>0.4609 (14.1398, 14.5347)</td>
<td></td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.2989</td>
<td>0.4089 (14.1015, 14.4963)</td>
<td></td>
</tr>
</tbody>
</table>

Pooled SD = 0.544075

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>232.22 °C lam. temp.</td>
<td>30</td>
<td>14.3373</td>
<td>A</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.2989</td>
<td>A</td>
</tr>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>13.814</td>
<td>B</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.
Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \)  \( SD_p = 0.544075 \)
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5233</td>
<td>22</td>
<td>0.8</td>
<td>0.802813</td>
</tr>
</tbody>
</table>

The sample size is for each level.

Figure A13 - Power curve for TPB sensitivity experiment 2 with data corrected.

TPB Sensitivity Experiment 2 T-Test

Two Sample T-Test Method

\( \mu_1 \): mean of Production Lamination Machine
\( \mu_2 \): mean of R&D Lamination Machine
Difference: \( \mu_1 - \mu_2 \)

Equal variances are assumed for this analysis.

Descriptive Statistics

<table>
<thead>
<tr>
<th>Sample</th>
<th>N</th>
<th>Mean</th>
<th>StDev</th>
<th>SE Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production Lamination Machine</td>
<td>29</td>
<td>14.757</td>
<td>0.279</td>
<td>0.052</td>
</tr>
<tr>
<td>R&amp;D Lamination Machine</td>
<td>30</td>
<td>14.278</td>
<td>0.461</td>
<td>0.084</td>
</tr>
</tbody>
</table>

Estimation for Difference

<table>
<thead>
<tr>
<th>Difference</th>
<th>SD_p</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4798</td>
<td>0.3824</td>
<td>(0.2804, 0.6792)</td>
</tr>
</tbody>
</table>
Test

Null hypothesis \( H_0: \mu_1 - \mu_2 = 0 \)
Alternative hypothesis \( H_1: \mu_1 - \mu_2 \neq 0 \)

<table>
<thead>
<tr>
<th>T-Value</th>
<th>DF</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.82</td>
<td>57</td>
<td>0.000</td>
</tr>
</tbody>
</table>

TPB Sensitivity Experiment 3

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>14.751</td>
<td>15.154</td>
<td>15.289</td>
<td>1.431</td>
<td>0.538</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>30</td>
<td>29</td>
<td>1</td>
<td>14.457</td>
<td>14.666</td>
<td>14.969</td>
<td>1.373</td>
<td>0.513</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>30</td>
<td>0</td>
<td>14.390</td>
<td>14.589</td>
<td>14.771</td>
<td>1.122</td>
<td>0.381</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis All means are equal
Alternative hypothesis Not all means are equal
Significance level \( \alpha = 0.05 \)

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>Adj SS</th>
<th>Adj MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>3.309</td>
<td>1.65440</td>
<td>16.83</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>86</td>
<td>8.455</td>
<td>0.09831</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>88</td>
<td>11.764</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>15.0231</td>
<td>0.3487</td>
<td>(14.9093, 15.1369)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>29</td>
<td>14.6362</td>
<td>0.3394</td>
<td>(14.5204, 14.7519)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.5975</td>
<td>0.2425</td>
<td>(14.4837, 14.7113)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.313547
Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>30</td>
<td>15.0231</td>
<td>A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>29</td>
<td>14.6362</td>
<td>B</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>30</td>
<td>14.5975</td>
<td>B</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \quad SD_p = 0.313547 \)
Factors: 1 Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4256</td>
<td>12</td>
<td>0.8</td>
<td>0.818663</td>
</tr>
</tbody>
</table>

The sample size is for each level.

Figure A14 - Power curve for TPB sensitivity experiment 3.
FPB Sensitivity Experiment 1

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>23.560</td>
<td>24.364</td>
<td>25.805</td>
<td>4.547</td>
<td>2.245</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>18.964</td>
<td>19.635</td>
<td>19.878</td>
<td>1.759</td>
<td>0.914</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>16.385</td>
<td>17.031</td>
<td>17.288</td>
<td>2.071</td>
<td>0.902</td>
</tr>
</tbody>
</table>

ANOVA Method

- Null hypothesis: All means are equal
- Alternative hypothesis: Not all means are equal
- Significance level: $\alpha = 0.05$

Equal variances were assumed for the analysis.

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 203.2 μm pitch, 304.8 μm pitch, 406.4 μm pitch</td>
</tr>
</tbody>
</table>

ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>435.88</td>
<td>217.939</td>
<td>237.85</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>39</td>
<td>35.74</td>
<td>0.916</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>471.61</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>14</td>
<td>24.534</td>
<td>1.416</td>
<td>(24.017, 25.052)</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>14</td>
<td>19.484</td>
<td>0.544</td>
<td>(18.967, 20.002)</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>14</td>
<td>16.758</td>
<td>0.669</td>
<td>(16.240, 17.275)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.957234

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>203.2 μm pitch</td>
<td>14</td>
<td>24.534</td>
<td>A</td>
</tr>
<tr>
<td>304.8 μm pitch</td>
<td>14</td>
<td>19.484</td>
<td>B</td>
</tr>
<tr>
<td>406.4 μm pitch</td>
<td>14</td>
<td>16.758</td>
<td>C</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.
Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \quad SD_p = 0.957234 \)
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.776</td>
<td>2</td>
<td>0.8</td>
<td>0.975471</td>
</tr>
</tbody>
</table>

The sample size is for each level.

![Power Curve for One-way ANOVA](image)

*Figure A15 - Power curve for FPB sensitivity experiment 1.*

FPB Sensitivity Experiment 2

Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Count</th>
<th>N</th>
<th>N*</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Range</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>20.67</td>
<td>21.25</td>
<td>21.50</td>
<td>1.81</td>
<td>0.83</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>18.96</td>
<td>19.63</td>
<td>19.88</td>
<td>1.76</td>
<td>0.91</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>18.23</td>
<td>18.46</td>
<td>18.68</td>
<td>1.29</td>
<td>0.45</td>
</tr>
</tbody>
</table>

ANOVA Method

Null hypothesis All means are equal
Alternative hypothesis Not all means are equal
Significance level  \( \alpha = 0.05 \)

*Equal variances were assumed for the analysis.*

Factor Information

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>3 220.56 °C lam. temp., 232.22 °C lam. temp., 243.89 °C lam. temp.</td>
</tr>
</tbody>
</table>
ANOVA

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between</td>
<td>2</td>
<td>50.045</td>
<td>25.0224</td>
<td>107.13</td>
<td>0.000</td>
</tr>
<tr>
<td>Within</td>
<td>39</td>
<td>9.109</td>
<td>0.2336</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>59.154</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>14</td>
<td>21.147</td>
<td>0.541</td>
<td>(20.886, 21.408)</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>14</td>
<td>19.484</td>
<td>0.544</td>
<td>(19.223, 19.746)</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>14</td>
<td>18.5024</td>
<td>0.3346</td>
<td>(18.2412, 18.7637)</td>
</tr>
</tbody>
</table>

Pooled SD = 0.483292

Grouping Information Using the Tukey Method and 95% Confidence

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>220.56 °C lam. temp.</td>
<td>14</td>
<td>21.147</td>
<td>A</td>
</tr>
<tr>
<td>232.22 °C lam. temp.</td>
<td>14</td>
<td>19.484</td>
<td>B</td>
</tr>
<tr>
<td>243.89 °C lam. temp.</td>
<td>14</td>
<td>18.5024</td>
<td>C</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Power Curve Calculation

One-way ANOVA
\( \alpha = 0.05 \) \( \text{SD}_p = 0.483292 \)
Factors: 1  Number of levels: 3

<table>
<thead>
<tr>
<th>Maximum Difference</th>
<th>Sample Size</th>
<th>Target Power</th>
<th>Actual Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6446</td>
<td>3</td>
<td>0.8</td>
<td>0.996094</td>
</tr>
</tbody>
</table>

The sample size is for each level.

Figure A16 - Power curve for FPB sensitivity experiment 2

24
Appendix B: Experiment Settings

This appendix contains the apparatus, test programme and procedures necessary to repeat the compression, three-point bend and four point bend experiments described in Chapter 5 Measurement System Development. These are described as general procedures with experiment specific information given in Table B1 to Table B3. The kink diameter test and tensile test setting are omitted as full details are included in Chapter 5. Specimen preparation is carried out as described in Section 4.3 Specimen Preparation to the lengths specified in Table B1 to Table B3.

General Procedures

Apparatus

- Instron 5564 or similar
- Instron 2525-817 50 N load cell or similar.
- Instron 2712-019 250 N pneumatic grips or similar.
- Spirit level.
- Test fixture (see tables).

Test Programme

- Applies a preload of 0.50 N before beginning test at 0.017 mm/s.
- Test proceeds at constant compressive displacement (see tables).
- Test ends as defined in tables.
- Cross head returns to start position.
- Load cell auto balances.
- Data interval is 0.12 N, read every 100 ms.
Equipment Set-Up
1. Switch on both the Instron 5564 and computer connected to it.
2. Fit the load cell and pneumatic grips.
3. Load the fixtures into the upper and lower grips.
4. Check alignment of the fixtures of the loading anvil relative to the supporting anvil using the spirit level and/or alignment tool if included with fixture.

Test Procedure
1. Run automatic load cell calibration and balance operation.
2. Place specimen into the fixture.
3. Lower the crosshead until there is 0.4 to 0.5 N applied. This ensures that the specimen is well seated in/on the fixture.
4. Start the test.
5. Repeat steps 1 to 4 for all specimens in the sample.

Record Keeping
1. Apply adhesive tape to each specimen.
2. Write the specimen number on the tape.
3. Label a bag with the test date, manufacture date of the test specimens and the manufacturing or design parameter varied with its value.
4. Put all the specimens from the sample in the labelled bag.
5. Carry out data collection when all the specimens from a sample have been tested.
6. Create a folder with the test method name e.g. “TPB test”.
7. Create a subfolder with the test date e.g. “21 Feb 2020”.
8. Copy the results table into an Excel worksheet and save it in subfolder created in step 3 using the format shown in Figure.
9. Click on the “report” tab in the Bluehill software, click on the printer button and select “save as PDF”. Save the report as a PDF in the same folder as the Excel worksheet and with the same name.

10. Click on the “test” tab in the Bluehill software, click on the checkered flag icon to finish testing of current sample. Click “yes” and save the sample file in the same folder as the Excel worksheet and with the same name.
**Experiment Specific Information**

*Table B1 - Settings for axial loading experiments.*

<table>
<thead>
<tr>
<th></th>
<th>Functionality Experiment</th>
<th>Sensitivity Experiment 1</th>
<th>Sensitivity Experiment 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fixture</strong></td>
<td>Prototype axial loading test fixture</td>
<td>Optimised axial loading test fixture</td>
<td>Optimised axial loading test fixture</td>
</tr>
<tr>
<td><strong>Key variable</strong></td>
<td>Catheter product</td>
<td>Lamination temperature</td>
<td>Lamination temperature</td>
</tr>
<tr>
<td><strong>Specimen type</strong></td>
<td><em>Cat. A, Cat. B</em> and <em>Cat. C</em> proximal shaft</td>
<td><em>Cat. A</em> proximal shaft</td>
<td><em>Cat. A</em> proximal shaft</td>
</tr>
<tr>
<td><strong>Specimen length</strong></td>
<td>45 mm</td>
<td>45 mm</td>
<td>45 mm</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><strong>Rate of Displacement</strong></td>
<td>2.5 mm/s</td>
<td>2.5 mm/s</td>
<td>16 mm/s</td>
</tr>
<tr>
<td><strong>End of test criteria</strong></td>
<td>Kinking of test specimen</td>
<td>Kinking of test specimen</td>
<td>Kinking of test specimen</td>
</tr>
</tbody>
</table>
Figure B2 - Prototype axial loading test fixture (left) and optimised axial loading test fixture (right).

Table B2 - Settings for three-point bend experiments.

<table>
<thead>
<tr>
<th></th>
<th>Functionality Experiment</th>
<th>Sensitivity Experiment 1</th>
<th>Sensitivity Experiment 2</th>
<th>Sensitivity Experiment 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fixture</strong></td>
<td>Three-point bend fixture</td>
<td>Three-point bend fixture</td>
<td>Three-point bend fixture</td>
<td>Three-point bend fixture</td>
</tr>
<tr>
<td><strong>Key variable</strong></td>
<td>Reinforcement layer pitch</td>
<td>Lamination temperature</td>
<td>Lamination temperature</td>
<td>Lamination temperature</td>
</tr>
<tr>
<td><strong>Specimen type</strong></td>
<td>Cat. A proximal shaft</td>
<td>Cat. A proximal shaft</td>
<td>Cat. A proximal shaft</td>
<td>Cat. A proximal shaft</td>
</tr>
<tr>
<td><strong>Specimen length</strong></td>
<td>45 mm</td>
<td>45 mm</td>
<td>45 mm</td>
<td>45 mm</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>10</td>
<td>10</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Rate of Displacement</strong></td>
<td>0.05 mm/s</td>
<td>0.05 mm/s</td>
<td>0.05 mm/s</td>
<td>0.05 mm/s</td>
</tr>
<tr>
<td><strong>End of test criteria</strong></td>
<td>Buckling of test specimen</td>
<td>Buckling of test specimen</td>
<td>Buckling of test specimen</td>
<td>Buckling of test specimen</td>
</tr>
</tbody>
</table>
Table B3 - Settings for four-point bend experiments.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity Experiment 1</th>
<th>Sensitivity Experiment 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fixture</strong></td>
<td>Optimised four-point bend fixture</td>
<td>Optimised four-point bend fixture</td>
</tr>
<tr>
<td><strong>Key variable</strong></td>
<td>Reinforcement layer pitch</td>
<td>Lamination temperature</td>
</tr>
<tr>
<td><strong>Specimen type</strong></td>
<td><em>Cat. A</em> proximal shaft</td>
<td><em>Cat. A</em> proximal shaft</td>
</tr>
<tr>
<td><strong>Specimen length</strong></td>
<td>45 mm</td>
<td>45 mm</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>14</td>
<td>34</td>
</tr>
<tr>
<td><strong>Rate of Displacement</strong></td>
<td>0.05 mm/s</td>
<td>0.05 mm/s</td>
</tr>
<tr>
<td><strong>End of test criteria</strong></td>
<td>3 mm compressive displacement</td>
<td>3 mm compressive displacement</td>
</tr>
</tbody>
</table>

Figure B4 - Optimised four-point bend fixture.

Figure B3 - Three-point bend fixture.
Appendix C: Finalised Measurement System

Based on the work documented in this thesis and the resulting findings, the composition of the finalised measurement system is defined in the following sections. The direct purpose of the measurement system is to measure the bending stiffness of a catheter shaft segment. The scope of this procedure is applicable to the proximal segment of the Cat. A catheter and similar. The results are analysed as per Section 3.7 Hypothesis Testing.

Apparatus

- Instron 5564 or similar machine capable of 0.05 mm/s compressive displacement.
- Instron 2525-817 50 N load cell or similar.
- Instron 2712-019 250 N pneumatic grips.
- FPB test fixture (see Appendix G: 3D Printed Fixture Drawings).
- Alignment tool.
- Precision ruler (300 mm).
- Cutting pliers.
- Digital microscope.
- Permanent marker.

Test Programme

- Applies a preload of 0.50 N before beginning test at constant compressive displacement rate of 0.017 mm/s.
- Test proceeds at constant compressive displacement rate of 0.05 mm/s.
- Test ends at 3 mm displacement.
- Cross head returns to start position.
- Load cell auto balances.
- Data interval is 0.12 N, read every 100 ms.
Procedures

Specimen Preparation
Prepare specimens as described in Section 4.3 Specimen Preparation to a length of 45 mm.

Equipment Set-Up
5. Switch on both the Instron 5564 and computer connected to it.
6. Fit the load cell and pneumatic grips.
7. Insert the loading anvil into the upper grip.
8. Insert the supporting anvil into the lower grip.
9. Check alignment of the loading anvil relative to the supporting anvil using the alignment tool.

Test Procedure
6. Run automatic load cell calibration and balance operation.
7. Place specimen centrally on the supporting anvil.
8. Lower the loading anvil onto the specimen using the fine adjuster for height. Stop when the loading anvil touches the specimen and there is less than 0.5 N applied.
9. Start the test.
10. Repeat steps 2, 3 and 4 for all specimens in the sample.

Record Keeping

Specimen Collection
11. Apply adhesive tape to each specimen.
12. Write the specimen number on the tape.
13. Label a bag with the test date, manufacture date of the test specimens and the manufacturing or design parameter varied with its value.
14. Put all the specimens from the sample in the labelled bag.

Data Collection
15. Carry out data collection when all the specimens from a sample have been tested.
16. Create a folder with the test method name e.g. “FPB test”.
17. Create a subfolder with the test date e.g. “21 Feb 2020”.
18. Copy the results table into an Excel worksheet and save it in subfolder created in step 3 using the format shown in Figure.
19. Click on the “report” tab in the Bluehill software, click on the printer button and select “save as PDF”. Save the report as a PDF in the same folder as the Excel worksheet and with the same name.

20. Click on the “test” tab in the Bluehill software, click on the checkered flag icon to finish testing of current sample. Click “yes” and save the sample file in the same folder as the Excel worksheet and with the same name.
Appendix D: Fractographic Examination

Specimen 1

Figure D1 - The SEM examination of specimen 1 identified the presence of two crack initiation zones. The areas imaged at higher magnification are indicated [8].
Figure D2 - SEM image of specimen 1, area 1 at higher magnification. Area 1 corresponds to a crack origin positioned within the middle of the extrusion wall. The crack origin corresponds to a discontinuity resulting from the edge of the reinforcement layer. The crack origin exhibits a relatively smooth morphology with some signs of micro ductility [8].

Figure D3 - SEM image of specimen 1, area 2 at higher magnification. Area 2 corresponds to a second crack origin. The features indicate crack initiation in the mid-wall of the extrusion at the interface between the reinforcement and outer layers [8].
Figure D4 - SEM image of specimen 1, area 3 which corresponds to a union of the two cracks originating at area 1 and area 2 [8].

Figure D5 - SEM image of specimen 1, area 4 which corresponds to the second union of the two cracks originating at area 1 and area 2 [8].
Specimen 2

Figure D6 - The SEM examination of specimen 2 identified a single crack initiation zone on the outside diameter on the outer layer (area 1). The areas imaged at higher magnification are indicated [8].

Figure D7 - Image shows specimen 2, area 1, the crack initiation zone at higher magnification. The crack origin exhibits characteristics of mechanical overload. Evidence of micro ductility is present [8].
Figure D8 - SEM image showing specimen 2, area 2. The features are indicative of counter-clockwise crack propagation and the groove in the material represents the interface between the reinforcement layer and outer layer [8].

Figure D9 - SEM image showing specimen 2, area 3, the second mid-fracture location. The features are indicative of clockwise crack propagation [8].
Figure D10 - SEM image showing specimen 2, area 4 which is another mid-fracture location. Some localized deformation is present associated with overload [8].

Figure D11 - SEM image showing specimen 2, area 5, the final fracture zone. A crack union associated with localised mechanical overload is present. Substantial ductility in the form of deformation is evident [8].
Figure D12 - The SEM examination of specimen 3 identified the presence of two crack initiation sites (area 1 and area 2) that are close together. The areas imaged at higher magnification are indicated [8].

Figure D13 - SEM image of specimen 3 showing area 1 and area 2. These areas represent the crack origin [8].
Figure D14 - Higher magnification of specimen 3, area 1. The crack initiated at the interface between the reinforcement layer and the outer layer [8].

Figure D15 - Higher magnification of specimen 3, area 2, the second crack initiation site. The crack initiated at the interface between the reinforcement layer and the outer layer [8].
Figure D16 - Specimen 3, area 3 shows localised ductility from removal of the reinforcement layer during failure [8].

Figure D17 - SEM image showing specimen 3, area 4 which displays minimal evidence of micro ductility [8].
Figure D18 - SEM image showing specimen 3, area 5 indicated by yellow. Some evidence of micro ductility is present [8].

Figure D19 - SEM image showing specimen 3, area 6, the final fracture zone corresponding to a union between the clockwise and counter-clockwise crack propagation. Substantial ductility is present in the form of deformation [8].
Appendix E: International Conference on Biotechnology, Bioengineering and Biological Solutions

The following is a paper previously submitted by the author as part of the 14th International Conference on Biotechnology, Bioengineering and Biological Solutions which took place on February 10-11, 2020 in Barcelona, Spain. The paper entitled “Test Method Development for Evaluation of Process and Design Effect on Reinforced Tube” is published in World Academy of Science, Engineering and Technology. The author received the “Best Presentation” award the certificate of which is also included in this section.