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# Title: The Quantification of Injectability by Mechanical Testing

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# Author Questionnaire

**1. Microscopy**: Does your protocol involve video microscopy, such as filming a complex dissection or microinjection technique? **N**

**2. Software:** Does the part of your protocol being filmed demonstrate software usage? **Y, filmed by videographer**

If **Yes**, we will need you to record using screen recording software to capture the steps. If you use a Mac, QuickTime X also has the ability to record the steps.

**3. Filming location:** Will the filming need to take place in multiple locations (greater than walking distance)? **N**

**Protocol Length**

Number of shots: **34**

# Introduction

1. **Introductory Interview Statements**

**REQUIRED:**

1.1. **Tom Robinson**: By measuring the force, we can ascertain whether a material is injectable and how changing the syringe or needle size, or the formulation chemistry and processing, affects the injectability **[1]**.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

**REQUIRED:**

1.2. **Erik Hughes**: This technique is fast and simple, can be used with most syringe-needle geometries, and requires little data processing to obtain key force values **[1]**.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

**OPTIONAL:**

1.3. **Tom Robinson**: This method is particularly applicable to injectable biomaterials, such as hydrogels and cements, for sustained drug delivery and regenerative medicine **[1]**.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

# Protocol

## 2. Mechanical Tester Setup

2.1. To set up the mechanical tester, attach flat compression testing platens to the mechanical tester **[1]** and manually equip the tester with a load cell with a maximum load of 200 Newtons **[2]**.

2.1.1. WIDE: Talent attaching platen(s)

2.1.2. Talent adding load to tester

2.2. Use the manual control buttons to separate the platens **[1]** to allow approximately 30 centimeters of space for the needle, syringe, and plunger **[2]**.

2.2.1. Talent using buttons/plates being separated *Videographer: Important step*

2.2.2. Shot of 30-cm space *Videographer: Important step*

2.3. To create a testing protocol, open the test wizard in the device software **[1]** and set the test type to uniaxial compression **[2]**.

2.3.1. Talent opening test wizard, with monitor visible in frame

2.3.2. SCREEN: Test type being set NOTE: All SCREEN shots were filmed by the videographer.

2.4. Set the measured force pre-load value at which the testing will begin and adjust the **speed to pre-load** to 5 millimeters/minute to set the speed at which the crosshead will move down until it encounters the pre-load **[1]**.

2.4.1. SCREEN: Pre-load value being set, then speed to pre-load being set

2.5. Set the **loading to displacement control** and select an appropriate test speed **[1]**.

2.5.1. SCREEN: Loading to displacement control being set, then appropriate text speed being set

2.6. Then set an **upper force limit** at which to stop the test **[1]**.

2.6.1. SCREEN: Upper force limit being set

## 3. Clamping System Setup

3.1. To set up the clamping system, attach two sets of clamps with grips large enough to securely ensconce the selected syringe to two stands **[1]**.

3.1.1. WIDE: Talent attaching clamp(s) to stand(s)

3.2. Place the grips between the crosshead and the baseplate with enough space below the grips for the syringe and needle **[1]** and line up the centers of the grips with the center of the crosshead. Use an empty syringe to help with the alignment **[2]**.

3.2.1. Shot of grips between crosshead and baseplate *Videographer: Important/difficult step*

3.2.2. Centers being lined up Vid NOTE: More action towards end of shot. *Videographer: Important/difficult step*

3.3. Then check that the clamps are secured firmly so that there is no movement in the clamps when a downward force is applied **[1]** and place a dish onto the bottom plate to collect the extruded material **[2]**.

3.3.1. Talent checking clamp(s) *Videographer: Important/difficult step*

3.3.2. Talent placing dish. Vid NOTE: Board not incremented should read 3.3.2 take 1. *Videographer: Important/difficult step*

## 4. Injectability Protocol

4.1. To perform an injectability experiment, insert the syringe into the clamp grips **[1]** and close the grips so that the syringe is held in place but can move up and down without resistance **[2]** with the syringe and plunger perpendicular to the crosshead **[3]**.

4.1.1. WIDE: Talent inserting syringe into grips *Videographer: Important step*

4.1.2. Shot of syringe in grips being able to move up and down *Videographer: Important step*

4.1.3. Shot of syringe and plunger perpendicular to crosshead *Videographer: Important step*

4.2. Use the buttons to lower the top plate just above the plunger **[1]** and click **Zero Force** to zero the measured force **[2]**.

4.2.1. Top plate being lowered

4.2.2. Talent clicking Zero Force

4.3. Then click **Run** to run the testing protocol **[1-2]**.

4.3.1. SCREEN: Run being clicked NOTE: Please cut before the final pop-up window appears

4.3.2. Added shot: Material being extruded from syringe. NOTE: Author thinks this is a more interesting shot, please show if possible

4.4. At the end of the test, raise the plates to a sufficient height such that the syringe can be removed **[1]** and repeat the test with the next sample **[2]**.

4.4.1. Talent raising plate(s)

4.4.2. Talent placing new syringe into grips

**5. Data Collection**

5.1. After each trial, save the data in a format such that table of force and displacement values can be generated **[1]** and plot the results from each trial with the displacement on the x-axis and the force on the y-axis **[2]**.

5.1.1. WIDE: Talent saving file, with monitor visible in frame

5.1.2. SCREEN: Results being plotted

5.2. When all of the trials have been plotted, determine the maximum **[1]** and plateau forces from each graph **[2]**.

5.2.1. LAB MEDIA: Figure 1B no text, arrow, bracket data line labels *Video Editor: please add Maximum text and arrow*

5.2.2. LAB MEDIA: Figure 1B no text, arrow, bracket data line labels *Video Editor: please add Plateau text and arrow*

# Protocol Script Questions

**A.** Which steps from the protocol are the most important for viewers to see?
2.2., 3.2., 3.3., 4.1.

**B.** What is the single most difficult aspect of this procedure and what do you do to ensure success?
3.2., 3.3. The most difficult thing to ensuring the clamps are secure and centered so that the syringe is perpendicular to the crosshead. This is done iteratively and can be checked with an empty syringe before sample testing begins.

 

# Results

## 6. Results: Representative Sample Curves

6.1. A typical force displacement curve consists of three sections **[1]** - an initial gradient, as the plunger overcomes the friction from the barrel and the material is accelerated **[2]**, a force maximum **[3]**, and a plateau, as the material is extruded at a steady state **[4]**.

6.1.1. LAB MEDIA: Figure 1B
6.1.2. LAB MEDIA: Figure 1B *Video Editor: please emphasize section of data line indicated by bracket and/or add bracket and text*
6.1.3. LAB MEDIA: Figure 1B *Video Editor: please emphasize section of data line indicated by Maximum row and/or add Maximum text and arrow*
6.1.4. LAB MEDIA: Figure 1B *Video Editor: please emphasize section of data line indicated by Plateau row and/or add Plateau text and arrow*

6.2. For viscous samples passing through a more narrow orifice **[1]**, the force needed to inject the sample at constant speed is greater than the force required to overcome the friction in the barrel and to accelerate the material **[2]**. Therefore, no distinct peak is observed **[3]**.

6.2.1. LAB MEDIA: Figure 1C
6.2.2. LAB MEDIA: Figure 1C *Video Editor: please emphasize section of data line indicated by bracket and/or add bracket and text*
6.2.3. LAB MEDIA: Figure 1C *Video Editor: please emphasize section of data line indicated by Plateau row and/or add Plateau text and arrow*

6.3. For highly viscous samples or very narrow needles **[1]**, the force required to extrude the material may be so great that the syringe buckles and fails **[2]**, often with very little extrusion of the material **[3]**.

6.3.1. LAB MEDIA: Figure 1D
6.3.2. LAB MEDIA: Figure 1D *Video Editor: please emphasize data line from zero to Syringe failure peak*
6.3.3. LAB MEDIA: Figure 1D

6.4. If the material being injected contains particles or is beginning to set **[1-TXT]**, filter pressing or bulk setting may occur **[2]**, leading to an incomplete injection **[3]**.

6.4.1. LAB MEDIA: Figure 1E **TEXT: *e.g.*, cement**

6.4.2. LAB MEDIA: Figure 1E *Video Editor: please emphasize inverted peak indicated by arrow and/or add arrow and Bulk Setting text*

6.4.3. LAB MEDIA: Figure 1E

# Conclusion

**7. Conclusion Interview Statements**

7.1. **Erik Hughes**: It is essential to make sure that the clamps are firmly secured so that the syringe fits snugly, is centered, and is perpendicular to the crosshead **[1]**.

7.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera (3.2.)

7.2. **Tom Robinson**: A correlation can be used to relate the measured force with the ease of injection. Alternatively, rheology can be used to understand how the process of injection affects the material **[1]**.

7.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera