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# The Effect of Jet Parameters on Jet Injection

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*Abstract*— **Current jet injection devices often utilize compressed air or springs to create a high-pressure fluid jet capable of piercing the skin. However, these devices are limited to a single invariable injection profile based on the impulse created by the compressed air or spring and therefore the parameters that affect injection are not well understood. To determine the effect of injection parameters on jet injection into tissue, including the effect of the fluid ejection profile on the injection, a controllable jet injection device was used to perform experiments into sheep and pig tissue. This paper demonstrates the importance of an initial peak in injection pressure and a subsequent lower follow-through pressure for successful jet injection into sheep and pig tissue.**

## I. Introduction

JET injection was first described by Hingson and Hughes as a drug delivery method that would make traditional needle injections obsolete [1]. They note "the fact that extremely fine high pressure jets are capable of piercing the human skin," and provide patient testing that showed jet injections were capable of delivering a skin analgesic and controlling diabetes in a patient for 2 weeks.

Since Hingson and Hughes published their paper in 1947, papers have appeared in the literature describing the benefits and complications with jet injection [2]-[4]. Some papers note that jet injections can be painful [2], [3], and others raise concerns about the consistency of injections [2], [4]. However, it was only recently that analysis of the mechanics of jet injection were studied, working towards a greater understanding of jet injection and the parameters that need to be designed into jet injection devices for optimal performance.

Baker and Sanders created a fluid mechanics model of a spring-powered jet injector [5] in 1999 which began the analysis of jet injectors as devices that could be optimized using engineering principles. Schramm-Baxter and Mitragotri published several papers [6]-[9] in this area. They also used a spring-based jet injector for their experiments but varied the nozzle diameter of their injector. The variation in nozzle diameter caused the exit velocity of the jet to change. Schramm-Baxter and Mitragotri measured the amount of fluid ejected (Q), the duration of the injection (t) and the cross-sectional area of the nozzle ($A_n$) to determine the average jet velocity during their experiments:

$$u_{jet}^{avg} = \frac{Q}{A_n t}. \quad (1)$$

They show a correlation between jet power of the fluid jet and injection penetration and dispersion as described by the equation

$$P_n = \frac{\pi}{8} \rho D_n^{\,2} u_n^{\,3}, \quad (2)$$

where increasing the jet power produces an increase in hole depth and maximum width of dispersion [7].

However, the Schramm-Baxter model only gives an average jet power based on an average jet velocity. Shergold et al. [10] hypothesize that there are two steps to needle-free injection: an initial penetration of the tissue and a subsequent delivery of the majority of liquid. Also, Shergold et al. noted that all needle-free syringes that they analyzed had a high-pressure pulse and then a decaying liquid pressure during the injection. These observations open the possibility that the optimal parameters may be different for each of these portions of the injection. It has been hypothesized that a high-pressure pulse (or "peak pressure") is necessary for formation of the initial tissue penetration [10]. This paper addresses the hypothesis that the delivery of the drug is mostly controlled by the subsequent lower jet pressure (also corresponding to a lower jet power).

## II. Materials & Methods

### A. Jet Injector

Experimentation was performed using the controllable Lorentz-force actuated needle-free injector (Figure 1) developed at the MIT BioInstrumentation Lab [11], [12].

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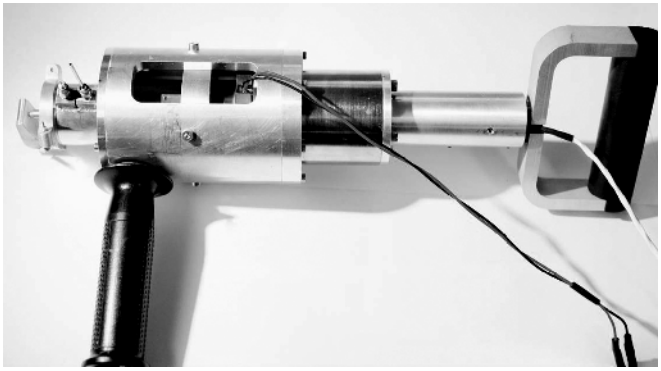

Fig. 1. A controllable Lorentz-force actuated jet injector designed in the MIT BioInstrumentation Lab [11], [12]. The injector is photographed upside-down so that the pressure sensor port and refill port are visible. The nozzle on the left-hand side of the device is covered with the nozzle cap in this image, normal procedure during filling of the device.

This jet injector is electrically controlled so that every millisecond of the injection profile (speed of fluid exiting the nozzle as determined by the pressure in the drug reservoir) can be programmed. The device also has integral pressure and piston position sensors, so that the pressure in fluid before it exits the nozzle can be measured. By measuring and recording the pressure, the exit velocity of the fluid can be estimated by Bernoulli's Equation,

$$u_n = \sqrt{\frac{2p}{\rho}}, \tag{3}$$

where $u_n$ is the fluid velocity at the nozzle (assuming a constant velocity profile) and $\rho$ is the density of the fluid. The Bernoulli Equation was compared with several friction models and found to best match the results of testing with the jet injector. This estimation of fluid velocity can be combined with the Baxter-Mitragotri model of jet power from Equation 2 to describe the instantaneous jet power of the injection with the Lorentz-force jet injector:

$$P_0 = \pi D_n^2 \sqrt{\frac{p^3}{8\rho}}. \tag{4}$$

### B. Formation of Injection Profiles

To test the importance of the jet power profile on the injection, a series of voltage waveforms were created to drive the Lorentz-force coil in order to create the desired jet parameters [11], [12]. These jet parameters included a variety of peak jet powers and a variety of follow-through jet powers. Through the software control of the Lorentz-force jet injector, each of these injection profiles could be saved and then recalled for use by opening the saved voltage waveform file.

### C. In-Vitro Injections

*In-vitro* injections were performed in excised sheep and pig tissue. The sheep tissue was harvested from a 5 month old dorset lamb and frozen at -80° C until use. Each sample was thawed at 4° C and then warmed to room temperature before experimentation. After injection the sample was chilled again at 4° C, cut down the midline of the injection and photographed. Analysis of the injection parameters was performed using a program written in Matlab [13].

Porcine belly tissue was purchased and frozen at -80° C until use. Each sample was thawed at 4° C and then warmed to room temperature before experimentation. After the experiments, the sample was frozen to -20° C, cut down the midline of the injection, and photographed. Once again, analysis of injection parameters was performed using Matlab.

All injections were performed at least 4 times for each set of parameters.

## III. Results

### A. Lamb Injections

To verify the Schramm-Baxter jet power hypothesis, injections were made into lamb tissue using two different nozzle diameters. Injection profiles were determined such that the jet power would be equivalent, as shown in Table 1.

TABLE 1
INJECTION PRESSURES FOR EQUIVALENT JET POWER INJECTIONS

| Noz. Dia. (μm) | Peak Pressure (MPa) | Peak Jet Power (W) | Follow-through Pressure (MPa) | Follow-through Jet Power (W) |
|---|---|---|---|---|
| 100 | 45 | 106.0 | 12 | 14.6 |
| 200 | 18 | 107.3 | 5 | 15.7 |

Injections into lamb tissue showed no significant difference between these injections, as shown in Figure 2.

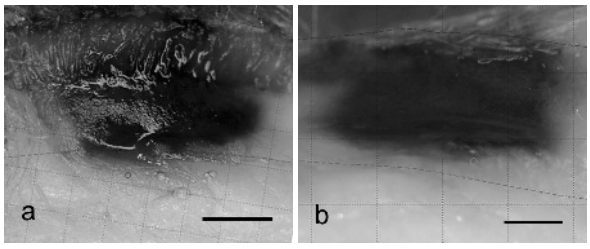


Fig. 2. Depth of injection into murine tissue is similar when using two different nozzle diameters each with an injection profile that produces the same jet power. Sample (a) was injected using a 100 μm nozzle and sample (b) was injected using a 200 μm nozzle using the injection pressures in Table 1 above. Scale bar equals 2mm.

Further injections were made to test the effect of increasing only the peak pressure on the injection results. Figure 3 shows that an increase in peak jet power from 70

W to 115 W, with similar follow-through powers of approximately 30 W, results in a deeper injection. Injections with a peak jet power of 70 W remain in the dermis while injections with a peak jet power of 115 W extend below the dermis and into the subcutaneous fat.

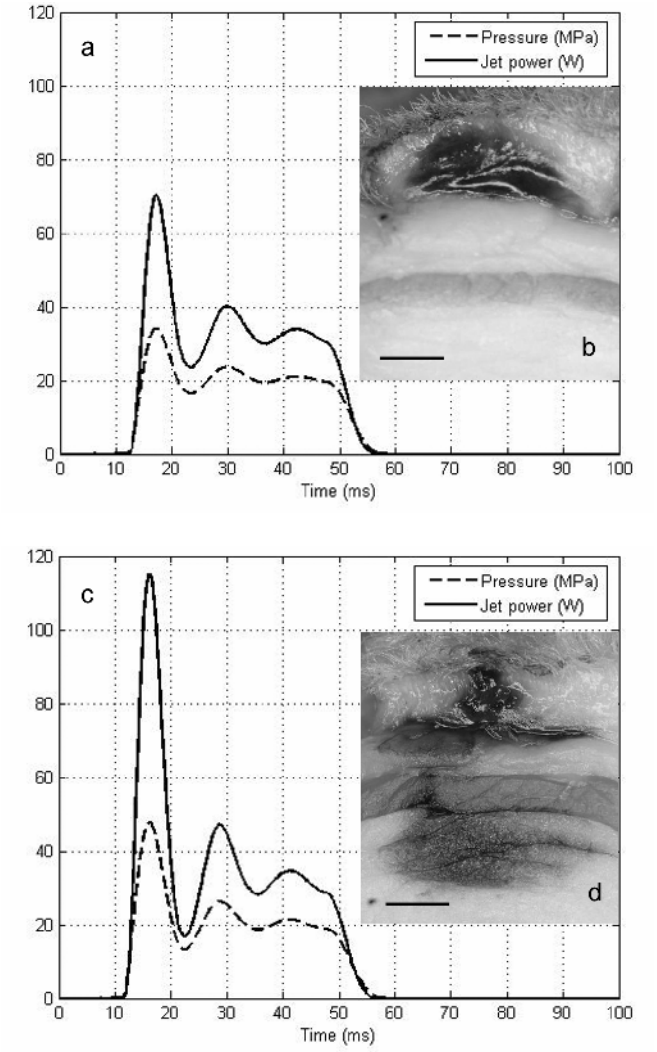


Fig. 3. (a) The pressure and jet power with a moderate peak pressure. (b) A sample of murine tissue injected using the profile shown in (a). (c) The pressure and jet power with a higher peak pressure than the profile shown in (a) but with the same follow-through pressure. (d) A sample of murine tissue injected using the profile shown in (c). Scale bar equals 2mm.

### *B. Porcine Injections*

Injections into porcine tissue were performed with the same peak pressure and various follow-through pressures as described in Table 2. The results, summarized in Figure 4, show that the majority of delivery of fluid occurs during the follow-through pressure phase. The lower pressure follow-through does not appreciably affect the depth of injection.

TABLE 2
PRESSURES FOR PORCINE INJECTIONS

| Noz. Dia. (μm) | Peak Pressure (MPa) | Peak Jet Power (W) | Follow-through Pressure (MPa) | Follow-through Jet Power (W) |
|---|---|---|---|---|
| 100 | 60 | 163.2 | 0 | 0.0 |
| 100 | 60 | 163.2 | 15 | 20.4 |
| 100 | 60 | 163.2 | 30 | 57.7 |

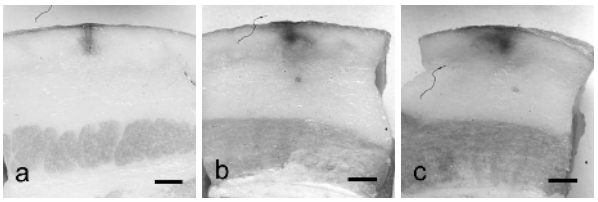


Fig. 4. (a) Injection into porcine tissue with a peak pressure of 60 MPa and no follow-through pressure, (b) injection using the same peak pressure and a follow-through of 15 MPa, and (c) injection using the same peak pressure and a follow-through of 30 MPa. Scale bar equals 2mm.

A statistical t-test was performed on the injection volume of the porcine samples (n=9). The volumes of fluid delivered using the 15 MPa follow-through and 30 MPa follow-through were significantly different ($p=0.008$ and $p=0.0003$, respectively) from the fluid delivered when the injection had no follow-through pressure.

## IV. DISCUSSION

The results from the experiments on murine tissue show that the depth of injection can be varied based on changing the peak pressure with which the fluid is ejected. Since jet power is proportional to pressure, increasing the pressure increases the jet power. These results agree with the Schramm-Baxter observations that the depth of injection increases with increasing jet power. However, the results do not yet describe a predictive model of the quantitative depth of injection based on jet power. As described by Shergold [10], the mechanical properties of the tissue will affect the ability of the jet to penetrate, so it can be expected that different quantitative models will be necessary for different tissue sources.

Experiments on injection dispersion into porcine tissue confirm the hypothesis that the primary injection depth is determined by the initial peak pressure and the majority of fluid delivery occurs during the follow-through pressure period. This knowledge is important for the design of future jet injectors or the creation of injection profiles for controllable jet injectors. In order to deliver less or more fluid to a certain depth in tissue, a jet injector should shorten or lengthen the follow-through pressure but not vary the initial peak pressure.

There may be further optimization of the follow-through pressure that can be explored in the future. It could be

possible that a pressure lower than the initial peak pressure may still have enough jet power to affect the depth of the injection. In the experiments described in this paper, the maximum follow-through pressure was only 33% of the peak pressure. Future experiments could focus on finding the maximum follow-through pressure that would not affect injection depth. Maximizing the follow-through pressure could allow for faster injections since more fluid could be delivered in a shorter period of time.

Also, future work may focus on developing a predictive model of depth of injection based on initial peak pressure. From the results presented in this paper, it appears that this model will be different for sheep and pig tissues, and it is expected that it would also be different for human tissue.

## V. Conclusion

We have shown that jet injection is based on two sequential steps: an initial peak pressure that determines the depth of injection and a subsequent lower follow-through pressure which delivers the majority of the fluid into the tissue. An increase in pressure during the initial peak pressure (corresponding to an increase in jet power) increases the depth of injection in murine tissue. Holding the peak pressure constant and adding increasing follow-through pressure increases the amount of fluid delivered to porcine tissue during a set period of time.

Future experimentation will focus on creating a quantitative model of depth of injection based on peak jet pressure and finding the limitations at the extremes of the peak and follow-through model. A full understanding of jet injection will allow for design of jet injectors that can fully deliver their drug to the appropriate depth, opening up this important drug delivery method for more applications.

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