INJECTION CHARACTERISTICS OF LIQUID JET FROM A NEEDLE FREE INJECTION DEVICE IN THE TISSUE SIMULANT

Kulachate Pianthong[1,*], Wirapan Seehanam[1], Wuttichai Sittiwong[1] and Brian Milton[2]

[1] Department of Mechanical Engineering, Faculty of Engineering, Ubon Ratchathani University, Thailand, 34190
[2] School of Mechanical and Manufacturing Engineering, University of New South Wales, Sydney, Australia, 2052
*Corresponding Author: E-mail: K.Pianthong@ubu.ac.th, Tel: +66-4535-3309, Fax: +66-4535-3308

Abstract

This study aims to investigate the dynamics characteristics of liquid jet injected from a needle-free injection device by analyzing the the flow visualization from the high-speed video camera and the CFD calculation. This is to investigate the jet flow phenomena (e.g. penetration, dispersion, velocity) in the quiescent air and in the tissue simulant (20% polyacrylamide gel) as the further information to apply in the real tissues. The jet injection parameters, which are jet velocity, piston movement, and jet penetration in the tissue simulant, for the needle-free jet injection, are thoroughly investigated by using the high-speed video camera and CFD simulation. In the experimental visualization, a high-speed video camera was used to capture the jet flow phenomena in the medium which are the quiescent air and the 20% polyacrylamide gel used as tissue simulant. Jet injection into the air, both in an experimental and numerical visualization, it is found that when the liquid volume ejected is decreased, the jet velocity slightly increases, and the average velocity of piston movement during jet injection process is found to be steadily decay over remaining 0.15 – 0. 2 m/s after the high velocity pulse during the first 1-10 ms. The CFD results show good agreement to results from experiments both quantitatively and qualitatively. Injecting into 20% polyacrylamide, the jet can be captured by the high speed video camera. The penetration process which consists of three stages which are the threshold stage, the penetrative stage, and the dispersion stage can be revealed.

Keywords*:* needle – free jet injection, CFD, tissue stimulant

1. Introduction

Jet injector delivers liquid medication or vaccine through a nozzle orifice via a high pressure, high speed narrow stream that penetrates the skin, as shown in Fig. 1. Drug or vaccine can be delivered to intradermal, subcutaneous, or intramuscular tissue depending on operating parameters performed by the jet injector device. The devices designed to deliver the drug were first developed in the 1940’s and were widely used for mass immunization campaigns from the 1950’s to the 1980’s [1-2]. It is believed that jet injection devices should improve the efficacy of the drug, due to better distribution in tissues where liquid drug delivered via jet injection is dispersed more widely; in addition, site pain after injection is very small, in a range of hundred micrometers. This mechanism was confirmed by J. Baxter's studies [3-4]. An important advantage of jet injectors over other novel needle-free drug delivery methods is that parenteral delivery of drug to the same sites as those used in needle and syringe delivery may allow for use of the same vaccine formulations with the same proven efficacy [2].

The device, there are many disadvantage of needle free jet injection device distributed in the market; therefore, the development have been required to improve efficiency of the jet injection method and the device. One study compared two alternative jet injector devices with standard device showed that the jet injector devices were associated with higher levels of pain and more local reactions; moreover, there is blood contamination in head of jet injection device after injection [1, 5]. This is because the device generates the liquid jet at high velocity and impact pressure resulting in blood splashed back from the patient [1, 2, 5]. For this reason, understanding on effects of the parameters on characteristics and behavior of needle-free jet injection for the completely controllable device has been essence to correctly specify the hole depth, created by the jet liquid jet, in the target tissue [2].

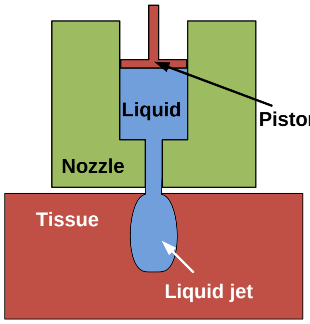

Fig. 1 Needle-free jet injection method

The devices have been concerned with injection efficiency corresponding to operating parameters which are jet penetration depth, liquid dispersion, jet velocity, volume ejected, and nozzle diameter. Jet power (Po) has been introduced as a combined parameter for those describing dependences and is calculated as:

$$P_o = \frac{1}{8}\pi\rho D_0^2 u_0^3 \qquad (1)$$

where D_0 is a nozzle diameter, u_0 is an exit velocity and ρ is a liquid density. In works of Joy Schramm-Baxtera et al. [3, 6] mentioned that with increasing the jet power, the shape of liquid dispersion at the end of the hole in simulant tissue is changed and jet penetration depth is increased. Further works [4] from this research group showed that depth of the injection hole increases with ejected volume before reaching an asymptotic volume. In addition, Shergold et al. [7] explored the penetration of a soft solid by a liquid jet injection from commercial needle-free jet injection devices, and revealed the discharge characteristic. A high pressure pulse, around 20-35 MPa, during the first 1-5 ms of injection, followed by steady decay in liquid pressure was found. However, those previous studies did not explore the jet generation behavior inside the nozzle during injection process, even though it directly affects on the characteristics of jet injection.

Therefore, in this study, the jet injection parameters, which are jet velocity, piston movement, and jet penetration in 20% polyacrylamide, for the needle-free jet injection, are thoroughly investigated by using the high-speed video camera and CFD simulation for the better understanding of needle-free jet injection process and providing useful information in the design of needle -free jet injection apparatus.

2. Material and Method

2.1 Experimental setup

Liquid jets, in these experiments, were produced from a commercial, spring-driven growth hormone jet injector, Cool Click (Bioject2000 Inc.) through an orifice of 0.17 mm in diameter. The maximum liquid volume ejected was 0.5 ml. In experiment, the jet is injected into the air and 20 % polyacrylamide gel, in which a nozzle tip attached the gel during the injection, and deionized (DI) water was used as the jet fluid. Optical setup, as shown in Fig. 2 was applied to visualize the jet flow phenomena and penetrative process in the gel. To gain a better understanding of the dynamics characteristics in time series, a high-speed video camera (Photron Fastcam SA5) was used to capture the jet flow phenomena in the medium and piston behavior during a jet ejection. During the operation process of the needle-free injection device, the frame rate of 15,000 frames per second (fps) was applied, and the major operating parameters, which are jet velocity, jet penetration, and piston movement is thoroughly investigated.

2.2 Experimental setup

20% Polyacrylamide gel were used as a model soft material which Young's modulus and hardness, reported by Schramm-Baxter et al. [6] are 0.22 MPa and 41 Hoo, respectively. The 20% gel was created by the addition of initiators (10% ammonium persulphate (APS) and N,N,N',N'-tetramethylethylenediamine (TEMED)) to a 40% (w/v) acrylamide solution. The acrylamide solution was mixed with DI water to create solutions possessing acrylamide concentrations in the range of 20% w/v, and the gel was polymerized by the addition of 60 ul 10% APS and 12 ul TEMED to the acrylamide solution of 6 ml.

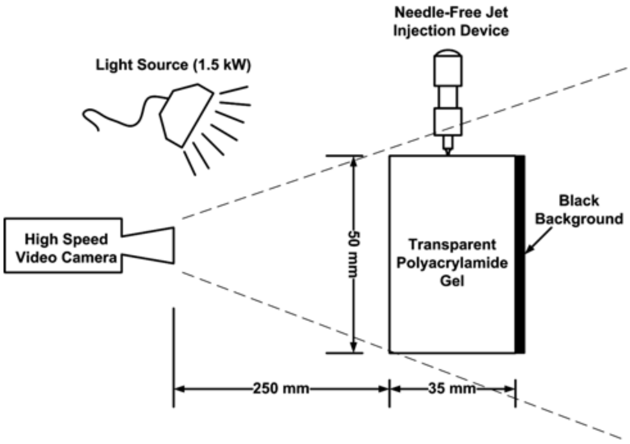

Fig. 2 Visualization setup

2.3 CFD modeling

From the mechanism of needle-free jet injection process, this setup can be modeled in a closed system domain with axi-symmetric geometry divided into two zone: nozzle cavity zone being full of dose liquid and air zone, as shown in Fig. 3. The CFD commercial code (FLUENT) is used as the tool to simulate the dynamic characteristics of the jet generation process. In the simulation, the two-fluid model consisting of liquid and air can be calculated by using the volume of fraction (VOF) model for interaction between fluid jet and air. The air and liquid density are simply specified to be compressible fluid by using the formula of ideal gas and compressible liquid including the instant liquid density, respectively. The turbulence model is the standard k-ε model with segregate solver for the non-linear equations. The velocity of the piston movement assuming as a moving wall during the injection is computed from the resulting force from the combination of spring, pressure, and friction forces acting on the piston in x-direction. The initial spring force can be calculated from Hooke's law equation where the spring force constant tested by using Rimac Spring Tester is around 17.8 kN/m.

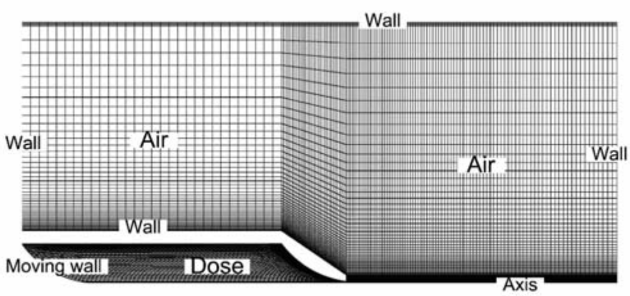

Fig. 3 CFD Modeling domain

4. Result and Discussion

4.1 Characteristics of the jet generation process

Dynamics characteristics of the piston and the jet injected into quiescent air, expressed as average velocities defined as its penetration distance along the medium divided by emerging time, are shown in Fig. 4 and 5. These figures show the results from the experiment and simulation. It is observed that water volume ejected is decreased, the jet velocity slightly increase, as shown in Fig. 4, and average velocity of piston movement during jet injection process, as shown in Fig. 5, is found to be steadily decay over remaining 0.15 – 0.20 m/s, before there is a high velocity pulse during the first 1-10 ms. This corresponds to the discharge characteristics, expressed as stagnation pressure, which was found by Shergold et al. [7]. However, it is observed that the average jet velocity trends from the both method are only slightly different; although, the CFD simulation gives higher average velocities than those from experiments. In the simulation, the phenomenon of the atomization is specified by simply VOF two phase flow model, and this causes the spray atomization, corresponding to dynamics drag, occurring jet injection into the air is not fully taken into account in the CFD model. This is in accord with the results shown in Fig 6. The thin jet can be found in CFD results while cloud of liquid atomization occurring around the jet during jet injection can be captured by a high-speed video camera.

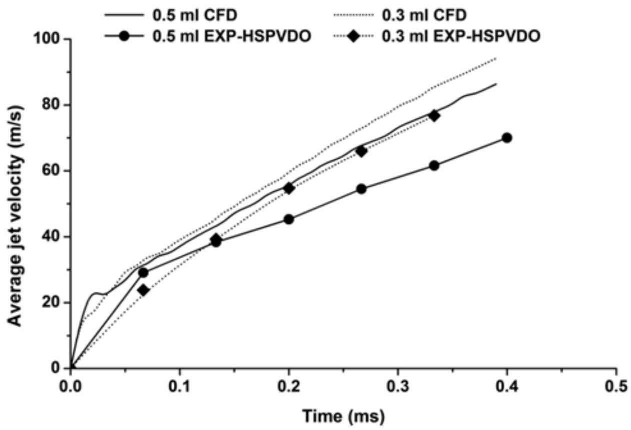

Fig. 4 Average jet velocities in quiescent air

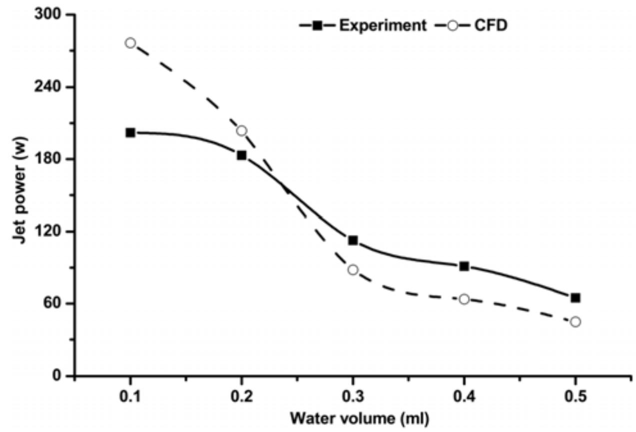

Fig 7 Jet power at various water volumes

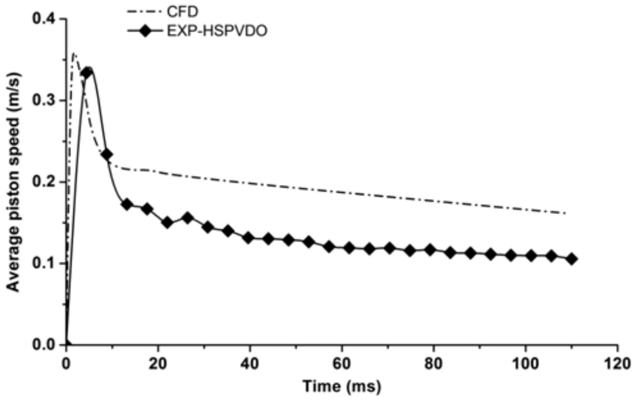

Fig. 5 Average piston speed

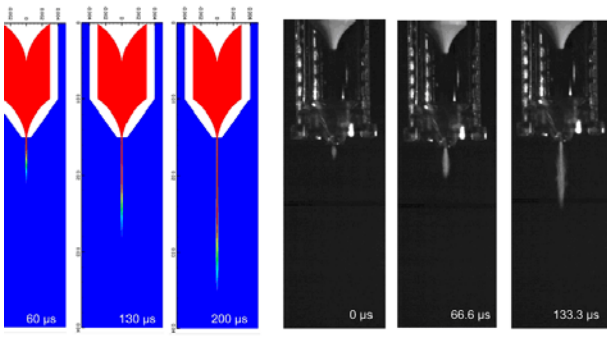

Fig. 6 Visualization of the jet ejected into the air

Fig 7 shows the effect of water volume on the jet power calculated by using equation (1) and the exit velocity resulted from experiment and CFD simulation methods. In both methods, it is observed that water volume ejected is increased, the jet power slightly decrease. This is because the exit jet velocity is decreased with the high injected volume. The initial injection pressure built up by first shock reflection near the nozzle exit is low with the high volume of column liquid. In addition, with the volume between 0.1 – 0.2 ml, the jet power given by CFD calculation is higher than by experiments. In contrasts to those injection volumes, experiment gives the results with higher power than the CFD result. The differences between the CFD and experiment results may come from the disintegration or atomization of the jet which is not fully taken into account in the CFD yet.

4.2 Characteristics of the penetrative process

From the experiment results, characteristics of penetrative process of the jet during the injection into polyacrylamide gel used as tissue stimulant are shown in Fig. 8 to Fig.

11. Fig. 8 shows the high speed video camera images for the penetration of the jet in 20% polyacrylamide, which the 0.4 ml volume of liquid retained inside a nozzle was used. From the visualization, three stages of the penetrative process can be observed. The first are the threshold stage which starts at initial movement of a compressing piston. The jet did not pierce through the gel surface (as shown in Fig. 8a-8j) because the impact pressure and the momentum of the jet at the initial stage did not exceed the surface threshold pressure of the gel. It is note that the short time of the threshold stage can be achieved with the low volume of ejected liquid as shown in Fig. 9 which presents penetration of 0.2 ml liquid jet.

For the second stage (penetrative stage), after the appropriate impact pressure and momentum, the jet can pierces through the gel surface and quickly penetrates the polyacrylamide gel as shown in Fig 8k-8l. In this stage, few dispersion of liquid and narrow hole can be observed. The last stage of the process is the dispersion stage which the penetrative velocity slightly is decreased while boundary of the liquid injected initially expands as shown in Fig 8m – 8u. This stage continuously operates along the injection process until completion.

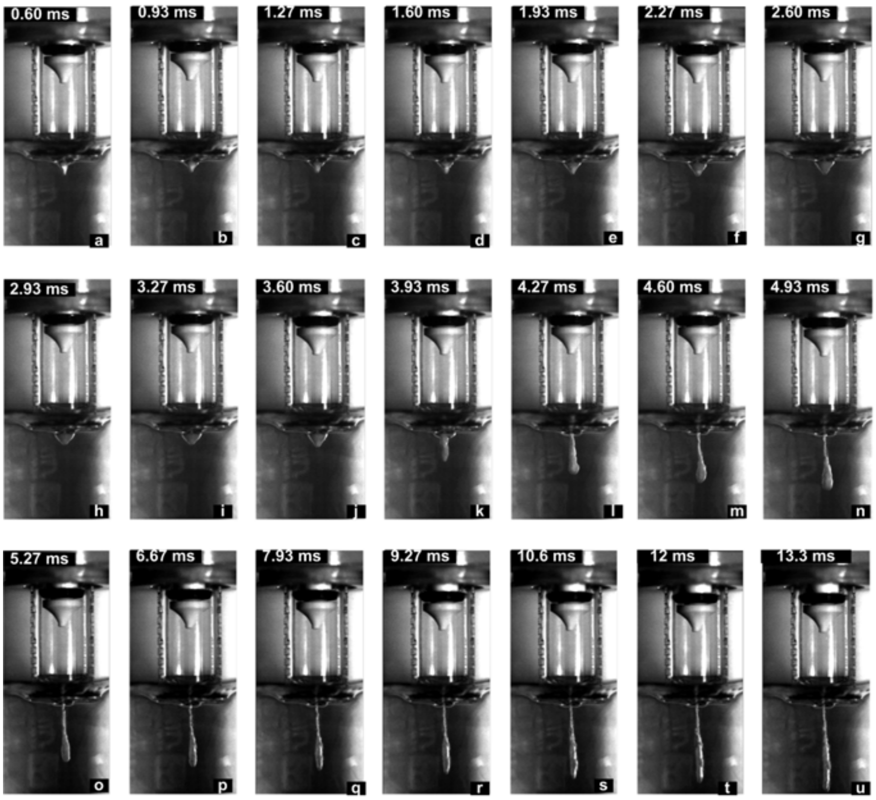

Fig. 8 Visualization of the 0.4 ml liquid jet (43.14 W of jet power) ejected into polyacrylamide

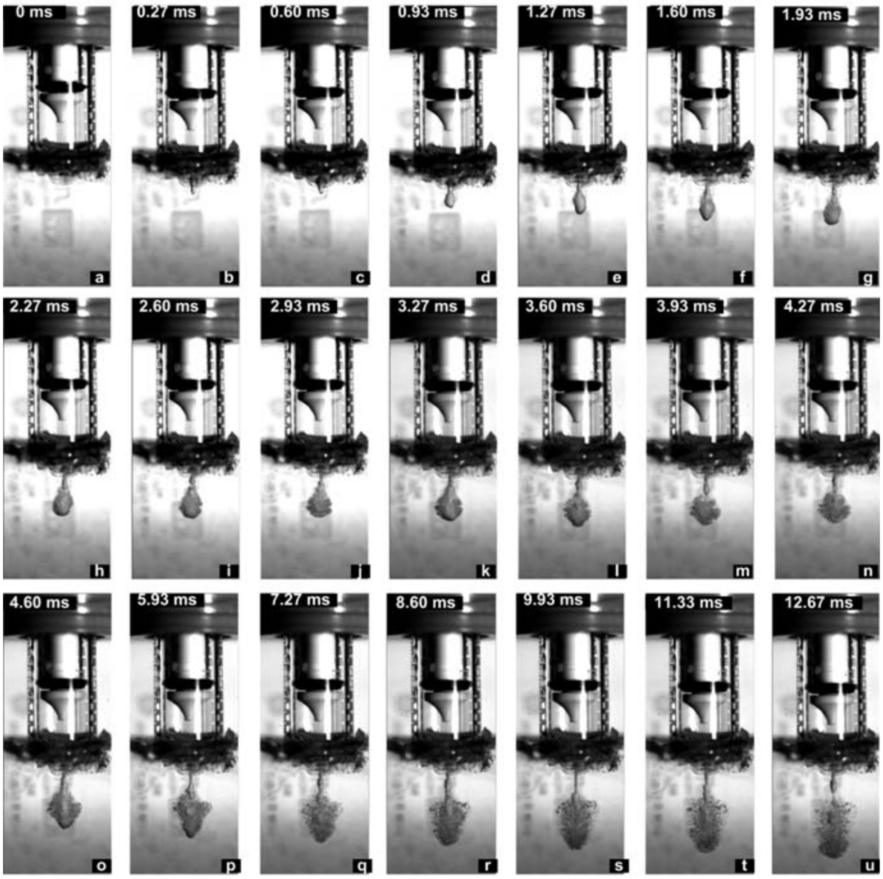

Fig. 9 Visualization of the 0.2 ml liquid jet (55.44 W of jet power) ejected into polyacrylamide

Usually, the penetrative process of jet injection mainly depends on the volume of retained liquid in a nozzle. Therefore, this study presents the influence of such volume on the penetration behavior. With volume of ejected water raging from 0.1 to 0.5 ml, Fig. 10 and 11 shows the averaged velocity and distance of liquid penetration. The velocity and distance correspond to the penetrative phenomena in Fig 8 and 9; the three stages of the penetrative process can be also found. At the threshold stage the average velocities is very high and suddenly decrease at initial injection before those velocities is quite constant as shown in Fig 10. This significantly relates to penetration distance which is reasonably constant at first 0 - 1 ms. It is note that the long time of the threshold stage can be achieved with the high volume of ejected liquid. This is because the momentum and velocity of the jet ejected from high liquid volume are small as described in the previous subsection. After that penetrative velocity is increased because the liquid can pierce through the gel surface and penetration distance more extends. This is at penetrating stage. Highest penetrative velocities in the injection process decrease with high ejected liquid volume. Because of the largely penetrated hole and high dispersion rate due to high injected mass. For the last as dispersion stage, the velocities slightly decrease to disperse the liquid into the medium.

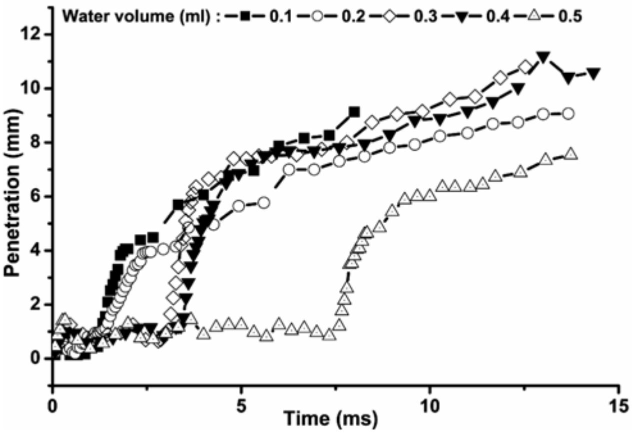

Fig. 10 Velocity of jet penetrating in polyacylamide

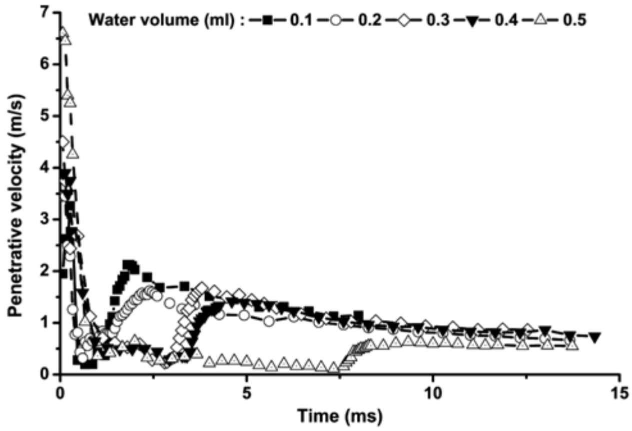

Fig. 11 Penetration of liquid jet in polyacylamide

5. Concluding remarks

In this study, the jet injection parameters, which are jet velocity, piston movement, and jet penetration in the tissue simulant, for the needle-free jet injection, are thoroughly investigated by using the high-speed video camera and CFD simulation. For the injection into the air, by using experimental and numerical visualization, it is found that liquid volume ejected is decreased, the jet velocity slightly increase, and the average velocity of piston movement during jet injection process is found to be steady decay over remaining 0.15 – 0. 2 m/s after the high velocity pulse during the first 1-10 ms. The CFD results show good agreement to the results from the experiment both quantitatively and qualitatively. For the injection into 20% polyacrylamide, the camera can capture the penetrative process which can be divided into three stages. These are the threshold stage, the penetrative stage, and the dispersion stage.

6. Acknowledgement

This work was granted by the Office of the Higher Education Commission and Thailand Research Fund (RTF), contract N0. RMU5180020, the National Research Council of Thailand (NRCT) through Ubon Ratchatani University Research Grant fiscal year 2007. Wirapan Seehanam was supported by CHE Ph.D. Scholarship.

7. References

[1] Giudice, E. L. and Campbell, J. D. (2006). Needle-free vaccine delivery, *Advanced Drug Delivery Reviews*, vol. 58, March 2006, pp. 68 - 89.

[2] O'Hagan, D.T. and Rappuoli, R. (2006). Novel approaches to pediatric vaccine delivery, *Advanced Drug Delivery Reviews*, vol.58, February 2006, pp. 29-51.

[3] Baxter, J. and Mitragotri, S. (2004). Needle-free jet injections: dependence of jet penetration and dispersion in the skin on jet power, *Journal of Controlled Release*, vol.97, April 2004, pp. 517-535.

[4] Baxter, J. and Mitragotri, S. (2005). Jet-induced skin puncture and its impact on needle-

free jet injections: Experimental studies and a predictive model, *Journal of controlled release*, vol. 106, July 2005, pp. 361-373.

[5] Jackson, L. A., Robert, G. A., Chen, T., Stout, R. and DeStefano, F., Gorse, G. J., Newman, F. K., Yu, O. and Weniger, B. G. (2001). Safety and immunogenicity of varying dosages of trivalent inactivated influenza vaccine administered by needle-free jet injectors, *Vaccine*, vol.19, June 2001, pp. 4703 - 4709.

[6] Baxter, J., Katrencik, J., Mitragotri, S. (2004). Jet injection into polyacrylamide gels: investigation of jet injection mechanics, *Journal of Biomechanics*, vol. 37, December 2004, pp. 1181-1188.

[7] Shergold, O. A., Fleck, N. A. and King, T. S. (2006). The penetration of a soft solid by a liquid jet, with application to the administration of a needle-free injection, *Journal of Biomechanics*, vol. 39, August 2006, pp. 2593 - 2602.