

## DEVELOPMENT OF NEEDLE-FREE JET WITH TWIN-FLUID ATOMIZATION PROCESSES

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**ABSTRACT** This paper investigates the development of the integrated twin-fluid micro-injector (IMA) to enhance the atomization performance and its penetration through the collagen gel with high speed micro-spray. Results showed that the IMA-type micro-injector produced the needle-free jets with diameter ranging from 23 $\mu$ m to 97 $\mu$ m depending on the gas pressure. It might be used to replace the metal needles for drug delivery through the skin. Results also found that the penetration of the micro spray to the collagen gel depends on the property of the working medium and the power of the impinging spray jet. The jet of single phase of gas flow did not result in the penetration into the collagen gel because its impinging power was less than the liquid phases. The working fluid with 5% levorotary C solution was more effective in the penetration test because of its surface reaction with collagen gel. The induction period and the break period were significantly reduced due to the higher injection power under the second injection mode. The maximum penetration depth was reduced for the collagen gel with higher concentration because the Young's modulus of the collagen gel increased with the higher collagen concentration.

**Keywords:** Needle-Free Jet, Micro Injector, Twin Fluid, Penetration, Atomization

### 1. INTRODUCTION

Micro-injector is normally fabricated by micro electrical discharge machining, laser machining process or MEMS machining process [1]. Atomization involves the processes of liquid-to-liquid, liquid-to-solid and liquid-to-gas transformations and has been widely applied in many scientific and engineering areas [2,3]. The industrial applications, such as the spray drying, the metal power production, the fuel spraying process, the spray cooling system and the printing and painting processes, etc. It is also used in the medical and cosmetic applications, such as the spray drug delivery, the needle-free drug delivery, and skin care, etc.

Needle-free drug delivery is an application of micro-injector [4]. Needle-free injector is used in drug delivery by applying a high speed and micro-jet to penetrate the skin [5]. The pumping of the needle-free injector through the syringe pump is similar to that of the conventional needles. The drugs were delivered through human skin and deposited in the dermal or subdermal region [6, 7]. The advantage of needle-free injection is its finer jet diameter as compared to that of the conventional metal needle ranging from 0.41mm to 0.71mm [8]. That's the reason why injection with the needle-free jet is less painful when the drug is injected into the skin.

Needle-free injection has been used for medical clinics and has been a commercial product since 1940's. As long as the needle-free injection is concerned, the control of the jet diameter and flow velocity is important in determining the injection power of drug delivery. However, the injection power of most injectors were supplied by the pressure type injectors. For example, Biojet Inc. and Schramm-Baxter, etc [4-8], developed the commercial injectors with the spring-driven device and produced jets with velocities of 100-200 m/s under a pressure higher than

136 bar (2000psi). It is clear that the pressure type injectors require extremely high pressure to overcome the high pressure drop of the liquid flow in the micro-channel to produce a high speed spray.

2003, Baik et al [9] developed the micro-diesel injector via LIGA processes. They fabricated 14 types of the micro-atomizer with varied geometries. The micro injector has multiple orifices with orifice number from 1 to 169 and diameters from 40 $\mu$ m to 260  $\mu$ m. Experimental results showed that the spray angle and the penetration velocity are determined by the overall area if the orifice instead of its number and geometric configuration. The spray angle and the penetration velocity decreased when the orifice area reduced. However, when operated at a higher pressure, the spray angle and the penetration velocity increased. Hence the droplet size reduced. 2004, Yang et al. [10] used deep-molding processes to fabricate pressure type-swirling micro-atomizers, including the X-ray LIGA process, ICP-LIGA process and injection molding LIGA process. The mean droplet size produced from these atomizers was still more than 20 $\mu$ m in their tests.

Micro-atomizers and injectors were widely used in the medical and engine applications. For example, 2002, Wissink et al. [11] used micro-atomizers for the pulmonary drug delivery application. They fabricated micro nozzle and micro sieve through MEMS processes. The orifice diameter and length of the micro-atomizer were 10 $\mu$ m and 1 $\mu$ m, respectively, to minimize the viscous effects. It produced spray with droplet size blow 20 $\mu$ m at pressures less than 5 bar. 2003, Hsu et al [12] further designed and tested a water-jet cutter for medical application. The characteristics and the modeling of the damage of tissue by the water jet were examined under various pressures as well as jet diameter. The experimental results showed that, under the same upstream pressure, the jet of larger orifice had higher exit dynamic pressure. The exit dynamic pressure decreases

as the distance between nozzle and pressure sensor was increased. The amount of decrease in dynamic pressure for the case with larger orifice was less than that of the case with small orifice. They also found that the depth cut by the water jet presented a linear relation to the water pressure. In the application to cut the pig liver by the vitro jet, it was observed that a jet with larger orifice diameter resulted in lesser isolation blood vessels on the liver. 2005, Ronald S. Weiss and Philip S. Li [13] further modified jet injection technique for local anesthesia of no-scalpel vasectomy without the use of a needle. It minimized the feeling of fear of vasectomy for a person involved in local anesthesia.

As for the supersonic micro-jet, Chen et al [14] fabricated a rectangular micro nozzle with distributed pressure measurements. It was designed to use in altitude control for mini satellites, micro satellites and nano satellites. Results showed that, for the same inlet and exit pressures, there is a closed supersonic area in the divergent region of the micro nozzle instead of the shock wave that usually occurred in the conventional-scaled nozzle. The phenomenon was attributed to the increased surface-to-volume ratio which led to higher viscosity dissipation in the micro nozzle.

Twin fluid atomizers have been designed to improve the atomization efficiency and reduce the droplet size in the conventional atomizers. Wang et al [15] had investigated the characteristics of the atomizer with internal impinging mechanisms. The SMD of the droplets below  $10\mu\text{m}$  has been achieved. The same mechanism was further applied to the design of the micro-atomizers [15-17]. They found the atomization efficiency was significantly improved. Results also indicated that the twin-fluid atomizer/injector performed better under lower pressure condition. For example, SMD reduced to  $5\mu\text{m}$  in a test under the gas pressure of 4bar.

In an effort to avoid the disadvantage associated with the pressure type injector, we attempted to develop the injectors with the twin-fluid atomization. The acceleration of the gas flow to a high speed is easier because the viscosity of gas medium is much lower than the liquid phase. It turns out that the velocity of gaseous flow exceeded  $300\text{ m/s}$  can be easily achieved under much lower pressure. Hence the development of the needle-free spray jet driven by high speed gas flow seems to be a promising choice in the engineering applications. In this paper, we designed a twin-fluid micro-injector with internal mixing mechanism for the applications in the needle-free drug delivery. This micro-injection device was designed with the integration of the micro-mixer and the micro-atomizer, called the IMA-type micro-injector. It allowed the mixing of different working fluids in the micro channels for specific medical applications. The penetration of the micro-spray into the collagen gel would be characterized.

## 2. EXPERIMENTAL SETUP

### 2.1 Experimental Facility and Instrumentation

The penetration of the needle-free spray jet into the collagen gel was studied by the image analysis of the spraying processes. The working fluids included pure water, 5% levorotary C solution, 70% aqueous glycerine and Nitrogen gas. The images of the penetration processes were taken by a high speed digital camera through a microscopy.

The experimental setup is shown in Figure 1. The test stand included a microscopy, a high speed digital camera, a syringe pump, a nitrogen gas supply system and light sources etc. Liquid was delivered from a syringe pump and gas supplied from a compressed nitrogen tank. The liquid and compressed nitrogen are supplied through the 4 mm tubes. The mass flow rate of liquid is controlled by the syringe pump.

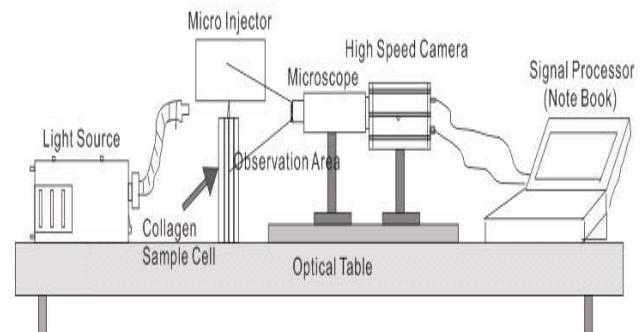


Fig.1 Schematic of experimental setup

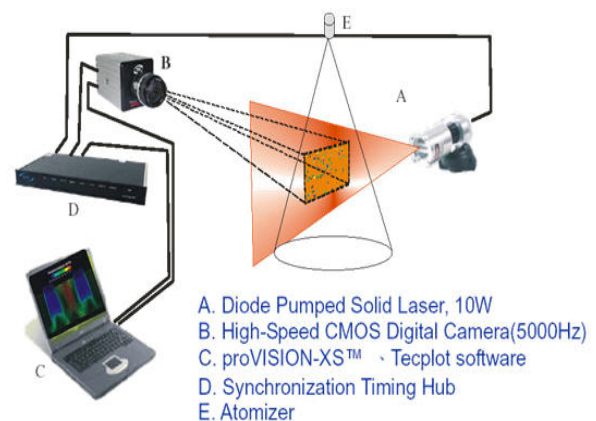


Fig.2 Schematic of the PIV system

The particle velocity is measured by an IDT/proVISION-XS Particle Image Velocimetry (PIV) system (see Fig.2). The PIV systems provide two-dimensional velocity images of the flow using whole field techniques based on imaging the light scattered by small particles in the flow illuminated by a laser light sheet. PIV measures whole velocity fields by taking two images shortly after each other and calculating the distance individual particles traveled within this time interval. From the known time difference and the measured displacement the velocity is calculated. This system works with a 10 W pulsed diode laser. The wave-length of the laser is  $795\text{nm}$ . The laser light is then transferred to a  $100\text{ mm}$  wide and  $0.3\text{ mm}$  thick laser sheet through a combination of spherical and cylindrical lens. The laser sheet is used to illuminate the flow field of the micro spray. High-speed CMOS digital camera captures two frames exposed by laser pulses. Maximum frame rate is  $5,145\text{ fps}$  with  $512 \times 512$  pixels resolution. The camera is synchronized with the laser beam and the frame grabber by means of a USB-2 Timing Hub.

The images are formed by two different layers, each of them containing information about the individual particles positions. These images were then post-processed by the Tecplot software in order to extract the sub-images formed by  $32 \times 32$  pixels from each layer and to perform a cross-correlation between the two corresponding sub-images. An interrogation algorithm extracts the correlation peak position from the cross-correlation domain with a sub-pixel precision, and performs the calculation of the two velocity components for those sub-images, by a pixel-to-mm conversion factor. Finally, the instantaneous velocity and average velocity plots are displayed by means of Tecplot software. Furthermore, the flow visualization technique is performed by the IDT-high speed camera system, an Olympus SZ-CVT microscope and a Nikon Coolpix 995 digital camera.

## 2.2 Configuration of the Micro-injector

The photo of IMA-type micro-injector is shown in Fig.3. The configuration of IMA-type micro-injector was designed with the central channel for the gas supply and the side channel for the liquid supply. The central channel was the main channel with the throat near the orifice. The cross sections of the throat and the orifice were  $450 \mu\text{m} \times 23.7 \mu\text{m}$  and  $500 \mu\text{m} \times 23.7 \mu\text{m}$ , respectively. It turned out that the hydraulic diameter of the orifice is  $38.3 \mu\text{m}$ . The side channel had two inlets and a micro-mixer providing the mixing mechanism for different liquids.

The material of the micro-injector was glass. It was low cost, feasible for thermal bonding and high hydrophilic property. It also possessed better mechanical properties and bounding strength. The dimension of the glass substrate is  $76 \times 26 \times 1 \text{mm}$ . The micro-injector was fabricated by the MEMS optical lithography processes.

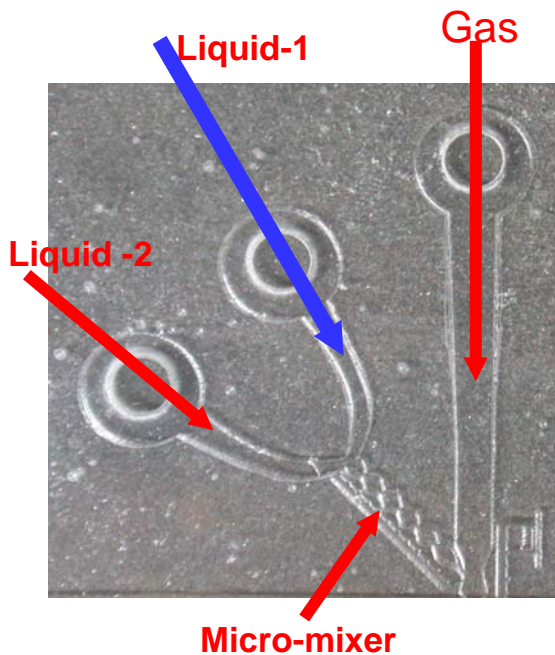


Fig.3、Photo of IMA-type injector

## 2.3 Characteristics of the micro-jet

Fig.4 showed the photo of the micro spray jet. It

looked like a needle type jet near the orifice, similar to the conventional metal-type needle. As shown in this photo, micro-jet diameter was  $24 \mu\text{m}$  and the length of the micro-jet was  $178 \mu\text{m}$ . According to the tests, the jet diameter varied from  $24 \mu\text{m}$  to  $97 \mu\text{m}$  depending on the gas pressure. It turned out that the diameter of the needle-free jet was less than that of the conventional needles which were normally much more than  $100 \mu\text{m}$ . Hence it was advised that the needle-free jets might be used to replace the metal needles for drug delivery through the skin.

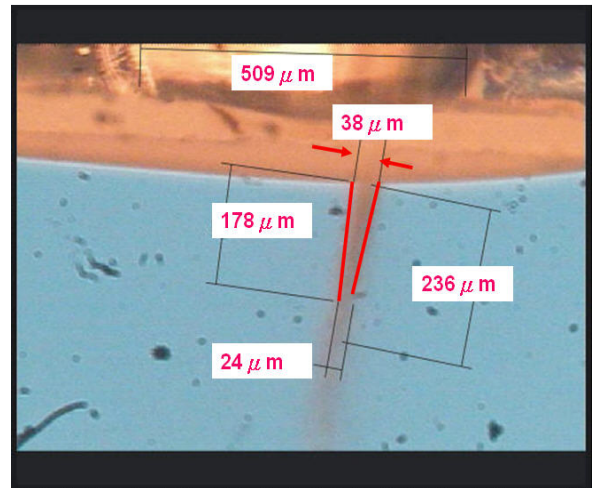


Fig.4 The photo of the micro jet  
( $P_g = 3.6 \text{bar}$ ,  $\dot{m}_l = 0.5 \text{g/min}$ )

## 2.4 Measurement of the mechanical property of Collagen gels

The collagen gels used in the research were prepared by mixing collagen powder with water. Concentrations of 12.5% and 15% of collagen were used in this research. Collagen Gels were put on the micro-MTS to measure the strain and the stress of the material. They were compressed by a cross-head with very slow speed. The relation between the applied pressure and deformation of the collagen gels was recorded. Results showed that the Young's modulus of 12.5% and 15% collagen gel were  $0.126 \text{MPa}$  and  $0.176 \text{MPa}$ , respectively.

## 3. EXPERIMENTAL APPROACH

### 3.1 Penetration of the micro-jet

As shown in Fig.1, the micro-injector was placed 2mm above the collagen gel. The penetration processes were taken by the high speed image system which consisted an optical microscope, an light source, a high speed digital camera and a computer. The procedure of the penetration test was listed as follows.

1. Adjust the test conditions including the atomization pressure and liquid flow rate.
2. Put the collagen gel under the micro-injector
3. Start the image acquisition system to record the penetration process
4. Analyze the duration and depth of jet penetration from the images.



### 3.2 Operations of IMA

There were two configurations for the needle-free drug delivery as shown in Fig 5. One fed liquid through the central channel and gas through the side channel. The other fed gas through the central channel and liquid through the side channel. Note that the hydraulic diameter of the central channel was larger than the side channels. The side channel had two inlets allowing two liquids with different viscosity to be fed into micro-injector simultaneously. The liquids were flown through the micro mixer and injected to the central channel. The test conditions were described as follows:

1. 1<sup>st</sup> injection mode: liquids were fed into the central channel, and gases fed into the side channel. Liquid mediums were 5% levorotary C solution and water, respectively.
2. 2<sup>nd</sup> injection mode: gases were fed into the central channel, and liquids fed into the side channel. Liquids were supplied as follows:
  - (a) Feed one inlet with 5% levorotary C solution, the other inlet with 70% aqueous glycerine.
  - (b) Feed both liquid inlets with water.

The viscosity of 5% levorotary C solution was 1.9cP. The viscosity of 70% aqueous glycerine solution was 38.8cP at 10°C.

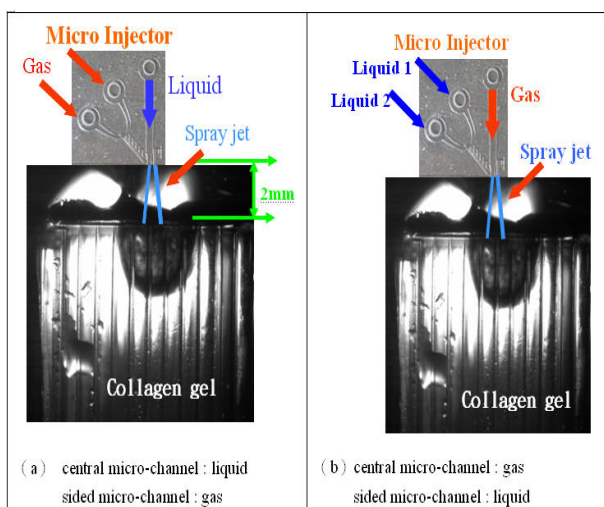


Fig.5 Schematic of two configurations of the needle-free drug delivery

## 4. RESULTS AND DISCUSSION

### 4.1 Micro-jet velocity measurement

Fig.6 shows the velocity distribution of the micro spray measured by PIV. Result showed that the spray was essentially the jet profile with central line velocity decreased from 13.5m/s to 5.5m/s at the positions 7mm to 26mm from the orifice. The information of the measuring points from 0mm to 7mm was not available because of the difficulties in the PIV measurements near the orifice.

However, the needle-free drug delivery was normally performed at 2mm from the skin. The jet velocity was very high at the exit of the injector. It was then decayed sharply in the downstream to the orifice.

Furthermore, the data measured by PIV was the velocity information of the bigger particles due to the limitation in laser power. Only the scattered light of big particles was recorded because their intensity was much higher than that of the finer particles. The velocity of big particles was slower than that of the fine particles because the particles were driven by the high speed gas flow. The relaxation time was much higher for the big particles.

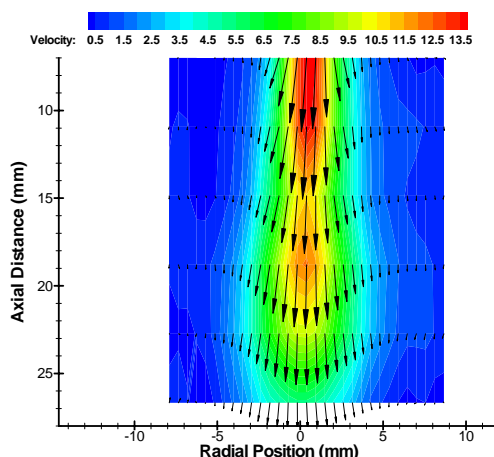


Fig.6 Velocity distribution of micro-spray  
( $P_g = 6\text{bar}$ ,  $\dot{m}_l = 1\text{ g/min}$ )

### 4.2 Impingement of gas jet on the collagen gel

Impingement of the gas jet from the micro-injector to the collagen gel was performed first to understand the influence of gas phase in the penetration processes. Fig.7 illustrated two configurations of the gas jet. One was the case of gas flow through the side channel with the central channel closed and the other was the case through the central channel with the side channel closed.

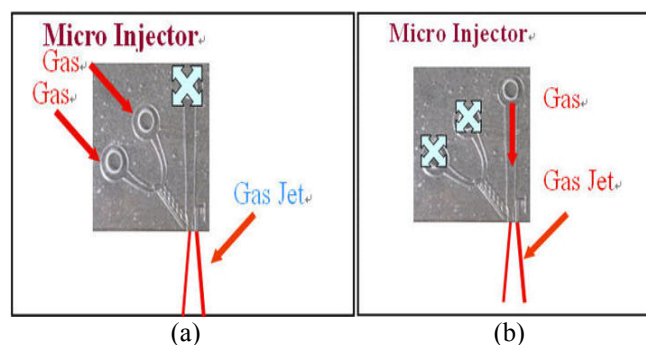


Fig.7 Penetration tests with single phase impingement  
(a) Gas supply from side channel, (b) Gas supply from central channel

Fig. 8 showed the photos of collagen gel by the gas jet impingement. The gas phase was supplied from the side channel in this case. Fig.8 (a) showed the surface condition of the collagen gel before gas impingement. The surface

was smooth in the beginning. As a comparison, Fig.8 (b) further illustrated the surface condition of the collagen gel after impingement by the gaseous jet. Deformation of the gel surface could be observed after the gas jet impingement. However, the gaseous jet did not result in penetration through the collagen gel surface even with long duration of gas impingement by 500sec. Similar result happened to the case of the gas jet supplied from the central channel (see Fig.9). Only deformation on the gel surface was observed even with long duration of gaseous impingement by 1000sec. No penetration through the gel surface occurred in the test.



Fig.8 Collagen gel with single phase impingement- gas flow through the side channel  
(a) Before gas impingement, (b) After gas impingement



Fig.9 Collagen gel with single phase impingement- gas flow through the central channel

#### 4.2 Penetration of micro impingement by 1<sup>st</sup> injection mode

Fig.10 showed the penetration of the spray jet through the Collagen gel with the first injection mode. The collagen concentration was 12.5% in this case. The dotted-line presented the result in the test when the central channel was fed with 5% levorotary C solution. The penetration processes could be described by two steps during micro-jet impingement. The first step was the induction period. The penetration was essentially the elastic deformation on the surface of the collagen gel. The second step was the surface break period. Significant penetration inside the collagen gel took place in this period. The surface of collagen gel deformed due to the jet impingement in the first duration of 0~25sec. The surface of the collagen gel began to break when micro-injection impact the gel after 25.5sec. The micro-jet continued to penetrate into the gel with a penetration depth of 6mm within 60 sec (see Fig.11).

Fig.10 also showed the penetration depth of collagen gel impinged by the micro water jet. The solid-line was the test result when the central channel was fed with water. There are two steps during micro-jet penetration. The induction period was longer (about 30sec). It followed a surface break period. The micro-jet continues to penetrate

into the gel until 42sec. The penetration depth was only 3.5mm in this case.

It seems clear that the penetration of the collagen gel depends on the property of the working medium and the power of the impinging spray jet. The jet of single phase of gas flow did not result in the penetration into the collagen gel because its impinging power was less than the liquid phases. The working fluid with 5% levorotary C solution was more effective in the penetration test because of its surface reaction with collagen gel.

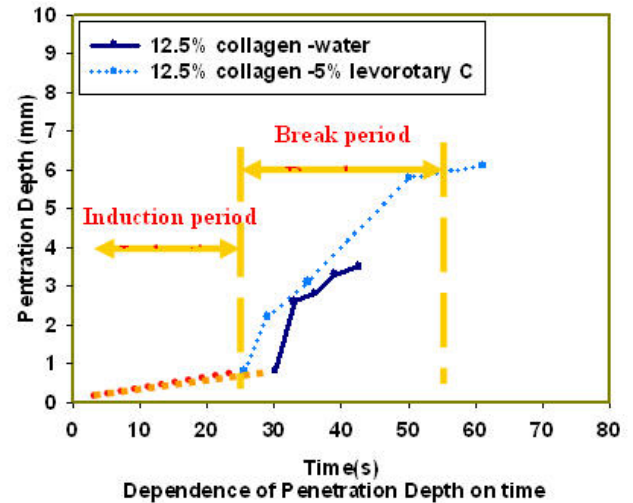


Fig.10 Penetration of the micro spray through the Collagen gel (12.5%) under 1<sup>st</sup> injection mode

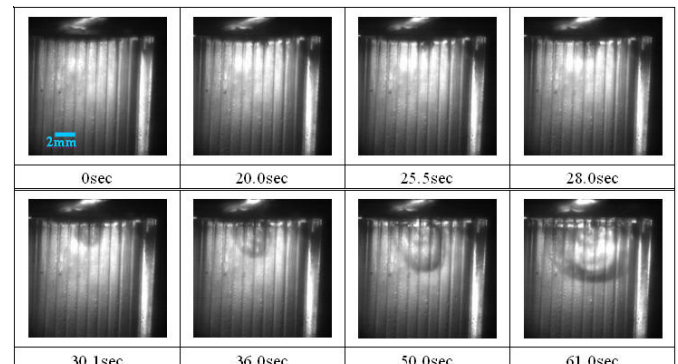


Fig.11 The evolution of micro-jet penetration:  
12.5% Collagen –5% Levorotary C Solution  
(1<sup>st</sup> injection mode)

Fig.12 further illustrated the test result of the case with 15% collagen gel. Similar results happened to this case. The penetration processes also divided by two steps during micro-jet impingement. The induction period had the duration of 30 sec and the break period was from 30 sec to 56 sec. The maximum penetration depth was 9.0mm under the impingement of the micro-spray with 5% levorotary C solution. On the other hand, the penetration depth with pure water impingement was only 3.8mm. It seemed clear that the addition of levorotary C has strong effect on the jet penetration, indicating the interaction between the collagen gel and the levorotary C.

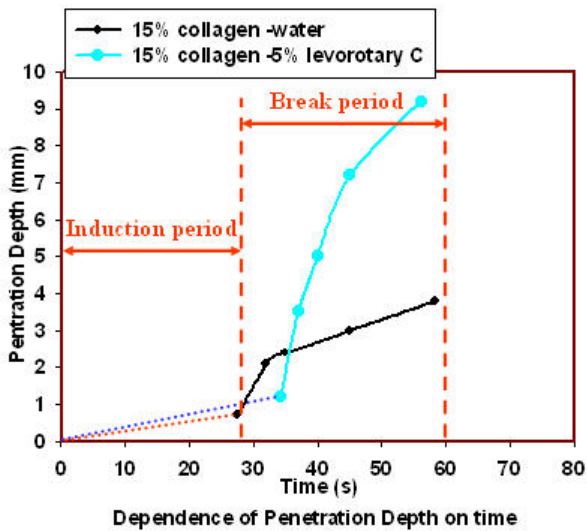


Fig.12 Penetration of the micro spray through the Collagen gel (15%) – 1st injection mode

#### 4.3 Penetration of micro impingement by 2<sup>nd</sup> injection mode

Fig.13 showed the result of penetration of collagen gel (12.5%) by the second injection mode. The solid line was the test result of the second injection mode when one liquid channel was fed with 70% aqueous glycerion solution and the other liquid channel fed with 5% levorotary C solution. There were two steps during the penetration. The induction period was reduced to 2.6sec in this case which was much shorter than the case with first injection mode. This was because of the increase in the injection power of the gas phase since the hydraulic diameter of the central channel for the gas flow was larger than the first case. The micro spray continued to penetrate into the collagen gel until 9sec. The penetration depth was 3.8mm as shown in Fig.13.

Fig.13 also showed the test result of collagen gel penetrated by micro water jet under the second injection mode. The dotted-line was the test result when the central channel was fed by water. The induction period was about 1.8sec. The micro-spray continued to penetrate into the gel until 9sec. The penetration depth was 6.5mm. It is concluded that the increases of hydraulic diameter of gas channel resulted in the reduction in the durations of the induction period as well as the surface break period.

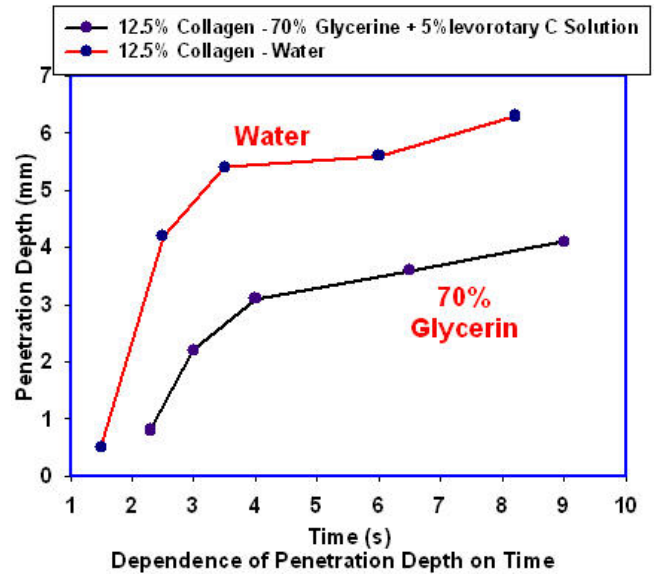


Fig.13 Penetration of the micro spray through the Collagen gel (12.5%) under 2nd injection mode

Fig.14 showed the result of penetration processes of the collagen gel (15%) under the second injection mode. The solid line was the test result when one liquid channel was fed with 70% aqueous glycerion solution and the other channel fed with 5% levorotary C solution. The induction period was 17sec. The surface break and the penetration periods continued from 17sec to 40sec. The maximum penetration depth was 5mm. Fig.14 further showed the test result of the penetration of the water spray into the collagen gel (15%) under the second injection mode. The central channel was fed with water. Results showed that the induction period and the break period were significantly reduced due to the higher injection power under the second injection mode. For example, the induction period was 2.5sec. The surface break and the penetration periods continued from 2.5sec to 24sec. The maximum penetration depth was 6mm. This result could be explained by the increase of the Young's modulus of the collagen gel with the higher collagen concentration.

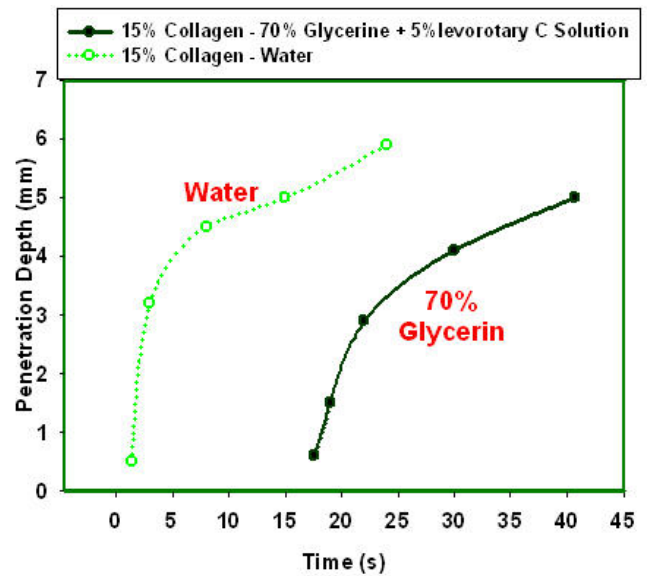


Fig.14 Penetration of the micro spray through the collagen gel (15%) under the second injection mode

## 5. CONCLUSION

The development of the IMA-type micro-injector produced the needle-free jets with diameter ranging from 23  $\mu\text{m}$  to 97  $\mu\text{m}$  depending on the gas pressure. It might be used to replace the metal needles for drug delivery through the skin. Results also found that the penetration of the micro spray to the collagen gel depends on the property of the working medium and the power of the impinging spray jet. The jet of single phase of gas flow did not result in the penetration into the collagen gel because its impinging power was less than the liquid phases. The working fluid with 5% levorotary C solution was more effective in the penetration test because of its surface reaction with collagen gel. The induction period and the break period were significantly reduced due to the higher injection power under the second injection mode. The maximum penetration depth was reduced for the collagen gel with higher concentration because the Young's modulus of the collagen gel increased with the higher collagen concentration.

## 6. ACKNOWLEDGEMENT

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## 7. NOMENCLATURE

$\dot{m}_l$	liquid mass flow rate	[g/min]
$p_g$	atomization gas pressure	[bar]
Z	axial distance	[mm]

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