# External Characteristics of Unsteady Spray Atomization from a Nasal Spray Device

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**ABSTRACT:** The nasal route presents an enormous opportunity to exploit the highly vascularized respiratory airway for systemic drug delivery to provide more rapid onset of therapy and reduced drug degradation compared with conventional oral routes. The dynamics of atomization at low injection pressure is less known as typical spray atomization studies have focused on industrial applications such as fuel injection that are performed at much higher pressure. An experimental test station was designed in house and an alternative method to characterize the external spray is presented. This involved the use of high-speed camera to capture the temporal development of the spray as it is atomized through actuation of the spray device. An image-processing technique based on edge detection was developed to automate processing through the large number of images captured. The results showed that there are three main phases of spray development (prestable, stable, and poststable) that can be correlated by examining the spray width. A comparison with a human nasal cavity is made to put into perspective the dimensions and geometry that the spray atomization produces. This study aimed to extend the current existing set of data to contribute toward a better understanding in nasal spray drug delivery. © 2013 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 102:1024–1035, 2013
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## INTRODUCTION

The efficacy of nasal spray drug delivery is mainly dependent on parameters such as drug formulation,[1,2] spray atomization,[3,4] spray device,[5] and patient handling.[6,7] Experimental and numerical studies in the literature for improved nasal drug delivery can be categorized into two fields: (1) external and internal characteristics of spray atomization from the nasal spray device,[8,9] and (2) transport and deposition of spray droplets in the nasal cavity.[10]

Experiments of the droplet deposition in the nasal cavity from nasal spray devices have been performed by Cheng et al.[11] wherein magnetic resonance imaging scans of a human nasal cavity was used to create a replica airway model. The results showed that the narrow airway passage in the nasal cavity limits the development of the spray plume and the dispersion of spray droplets inside nasal cavity. Furthermore, the study recognized the impact of inhalation flow rate and aerosol size on deposition efficiency. Suman et al.[12] allowed volunteers to operate nasal sprays that contained $^{99m}$technetium-labeled spray droplets. The regional deposition of spray droplets in nasal cavity was captured by gamma scintigraphy and the results concluded that the droplet size emitted from nasal spray bottle has a significant effect on drug delivery. Therefore, by controlling the droplet size distribution (DSD), targeted deposition patterns may be attained.

Dayal et al.[1] showed that the use of bioadhesive polymers (used to increase residence time and drug absorption) increases viscosity and also has an impact on the DSD. Furthermore, different drug formulations for therapeutic effects will also exhibit different fluid properties. Therefore, alternative means

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to control the DSD should be investigated to provide flexibility in drug developments. A study by Kippax et al.[6] using laser Doppler anemometry showed that different DSDs are produced for different actuation parameters that included actuation force and speed. The variation in actuation parameters is most evident among different age groups (e.g., child vs. adult), which has also been confirmed by Doughty et al.[13] This study presents actuation profiles and its variation against actuation force, hold force, and release force. The compression velocity, hold time, and release velocity of nasal spray nozzle and the average spray weight produced by adult and child users were correlated with the use of a linear displacement transducer. It should be noted that no actual DSD data were produced. However, the results are significant for correlating machine-actuated stations to real-life user actuations to provide *in vitro* bioequivalence testing of nasal aerosols as set out by the US Food and Drug Administration (FDA) draft guidance document.[14]

Guo and Doub[2] and then later Guo et al.[7] and Liu et al.[15] studied the influence of actuation parameters by an automated system, including shot weight, stroke length, and stroke velocity on the spray pattern and DSD. The actuation parameters were measured by electronic automated actuation system; spray external characteristics by high-speed camera and DSD were analyzed by laser diffraction system. Stroke length and actuation velocity are found to have significant impact on DSD and spray pattern, whereas the shot weight is the least sensitive characteristics to the variation of actuation parameters. Velocity profiling of nasal spray pumps were also performed by Williams et al.[16]

By studying the atomization process, DSD as well as spray characteristics such as spray velocity, angle, and penetration can be found. Recently, Inthavong et al.[17,18] applied particle image velocimetry and particle/droplet image analysis (PDIA) to study the continuous spray from nasal spray device. The study highlighted the importance of understanding local characteristics of spray development within its surrounding because the limitation of the narrow cross section of the nasal cavity does not allow the full development of a spray plume. The experimental studies reviewed provide important data for researchers using computational fluid dynamics (CFD) to simulate the transport and deposition of inhaled drug particles.[19–23] Such CFD studies have evaluated different spray delivery parameters (spray cone angle, droplet velocity, particle size, insertion angle, and particle release location) on deposition efficiency.[24,25]

The objective of this study is to extend the current set of data obtained in the author's earlier work[3] on the external characteristics of a nasal spray during a steady stream of flow. The work presented in this paper extends the previous study by investigating the atomization and spray development in a time-dependent mode. Furthermore, the difference is not only temporal, but also spatial because the spray is now ejected vertically upward in this study, which is more realistic in terms of a typical nasal spray operation performed by patients. An automated actuation system under different loads is also applied to simulate different strengths in actuation performance. Current methods for nasal spray characterization have used the laser diffraction technique to characterize the beginning, middle, and end of the plume, and such measurements should be made at three distances from the delivery orifice (FDA Guidance Draft). However, this study reports the use of high-speed photography, and image-processing algorithms that have been developed in house are used to determine the external spray characteristics including the three phases of plume development.

## METHODS

The experimental setup consists of an automated actuation system consisting of an actuation station that contains the spray device, a programmable logic control (PLC) unit, water supply, and a visualization

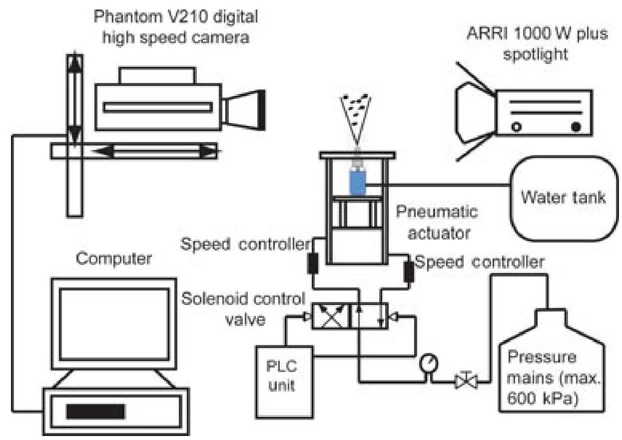


**Figure 1.** A schematic of the experimental setup showing the automated actuation system and the visualization system.

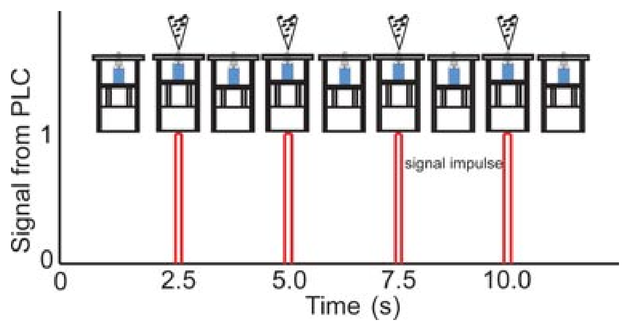


**Figure 2.** Signal profile sent from the PLC unit to activate/deactivate the control valves.